THE BRITISH JOURNAL OF [illegible]

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THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

NOVEMBER, 1950

COMMUNICATIONS

CONTROL OF EXPERIMENTAL INFECTION OF THE VITREOUS BY PENICILLIN*

BY

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London

ATTEMPTS to control experimental vitreous infections by the use of penicillin involve a clear understanding of the concentrations of penicillin made possible by different methods of application, and also an appreciation of the fact that to be effective treatment must be initiated before the vitreous becomes disorganized. In a series of earlier communications (Sorsby and Ungar, 1946; 1947; 1948a and b) it has been shown that levels of penicillin concentration in the vitreous were low after systemic administration of 50,000, 250,000, 500,000, and 1,000,000 units. The application of concentrated ointments (50,000 U/g.) likewise gave unsatisfactory results. The values obtained by the injection of 50,000 units subconjunctivally were also not high, but became significant

* Received for publication July 25, 1950.

when adrenaline 1 :1,000 was used as the solvent. A high level persisting for 48 hours was obtained by the direct intravitreal injection of 5,000 units, and levels almost as high and as persistent could be obtained by the injection of 1,000,000 units in adrenaline, 1 :1,000 subconjunctivally. The subconjunctival injection of 1,000,000 in water, or the retrobulbar injection of 1,000,000 units in either adrenaline or water, gave distinctly lower, though still tangible, levels. The Figure shows the more significant of these findings. On the basis of these studies, the best method of treatment would appear to lie between the direct intravitreal injection of 5,000 units and the subconjunctival injection of 1,000,000 units in adrenaline.

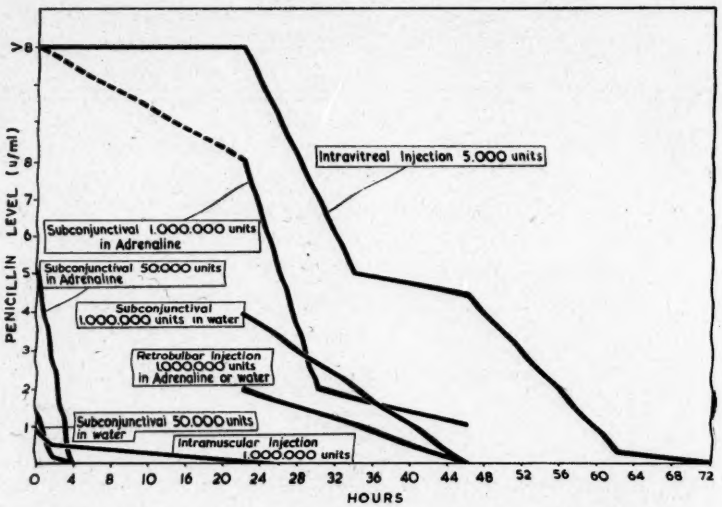

FIGURE.—*Levels of penicillin in the vitreous reached by different dosages and methods of administration (after Sorsby and Ungar, 1948a, Graph 2).*

Experimental studies (Sorsby and Ungar, 1946; 1948a, c) have shown that:

(*a*) vitreous infections do not respond well to intramuscular injections, and still less to the application of concentrated ointments, and although subconjunctival injections of 50,000 units gave satisfactory results, these were not uniform;

(*b*) direct intravitreal injections likewise gave inconstant and on the whole unsatisfactory results;

(*c*) preliminary trials with subconjunctival injections of 1,000,000 units gave promising results, but emphasized the need for early treatment. Treatment begun 24 hours after infection prevented panophthalmitis but left the vitreous as a grey organized mass.

Present Investigations

In the present study an attempt has been made to assess the value of retrobulbar and subconjunctival injections of penicillin, treatment being initiated either immediately after infection or 3 hours later.

Treatment by Retrobulbar Injection of 1,000,000 Units.—Rabbits weighing about 2 kg. each were used; 100,000 organisms of *Staph. aureus* 663 suspended in 0·05 ml. saline were introduced centrally into the vitreous.

The injection was made by the means of a tuberculin syringe into the right eye of each animal. Treatment consisted of retrobulbar injection of 1,000,000 units penicillin in 1 ml. water or adrenaline 1:1000. Two animals were used as controls, and four further batches of two animals each were first treated (*a*) immediately, (*b*) at 3 hours, (*c*) at 6 hours, and (*d*) at 12 hours after infection respectively.

The controls developed panophthalmitis within 48 hours and were destroyed. The course of events in the treated animals is recorded in Table I.

TABLE I

Retrobulbar Injection of 1,000,000 *Units Penicillin in* 1 *ml. Water or Adrenaline*

Infection: Intravitreal injection of 100,000 organisms *Staph. aureus* 663

Time of Treatment in Relation to Infection	Penicillin 1,000,000 units in 1 ml. water	Penicillin 1,000,000 units in 1 ml. adrenaline 1 : 1,000
Immediately and 24 hours after	*Rabbit A* died 2 days after	*Rabbit E* at 7 days cornea hazy, suppurative conjunctivitis at 17 days cornea opaque, suppurative conjunctivitis at 12 weeks eye normal except for small corneal scar
3 and 24 hours after	*Rabbit B* died 5 days after	*Rabbit F* at 7 days slight conjunctivitis, otherwise normal at 17 days normal at 12 weeks normal
6 and 24 hours after	*Rabbit C* at 7 days normal at 17 days normal at 12 weeks normal	*Rabbit G* at 7 days conjunctivitis, otherwise normal ; died on 13th day, eye normal
12 and 30 hours after	*Rabbit D* at 7 days conjunctivitis, otherwise normal at 17 days thin vitreous veil at 12 weeks normal	*Rabbit H* at 7 days conjunctivitis, otherwise normal; animal very ill, died the following day

It will be seen that four of the eight animals died during the course of the experiment. A post-mortem examination revealed no definite cause for these deaths. There was in particular no evidence of any generalized infection; as two of these deaths occurred early they prevented any assessment of the therapeutic effect of the injection on the vitreous infection. The results, as far as they went, suggested the following conclusions:

(i) Injections of 1,000,000 units penicillin in water retrobulbarly, given to one animal 6 hours after infection and 18 hours later, and to another animal 12 hours after infection and 18 hours later, were effective in controlling a heavy vitreous infection.

(ii) A similar dose of penicillin in adrenaline was effective in controlling the infection in the surviving animals in which it had been employed, irrespective of whether the first treatment was given immediately, or 6 hours after infection.

In this group of animals there was a severe conjunctival reaction and in one the cornea became opaque. These reactions proved transient and were apparently irritative in nature. These irritative phenomena are discussed more fully below.

Treatment by Subconjunctival Injection of 1,000,000 Units.

(*a*) Fifteen rabbits were used. The same infecting agent and mode of injection was employed but the dose was increased to 250,000 organisms suspended in 0·05 ml. saline. Three animals were used as controls. Six animals were treated by injections of penicillin at 3 hours and 24 hours after infection, and six received the same treatment with a third subconjunctival injection at 48 hours. The three control animals developed panophthalmitis within 36 hours and were destroyed. The course of events in the twelve treated animals is shown in Table II. It will be seen that six of the twelve animals had to be destroyed on the tenth day owing to severe conjunctival and corneal reactions, with which were associated considerable irritative lesions on the skin ot the lids and the surrounding areas. Clinically, the impression was gained that the ocular infection was under control, but the state of the animals did not warrant their being kept alive. Two possibilities had to be considered: that the severe intra-ocular infection was not controlled and produced heavy corneal reactions; or that the penicillin injections had proved irritating. The latter possibility proved to be true, as was shown by independent tests with another apparently pure sodium penicillin preparation. The significant finding is that all the six animals that were kept alive ultimately did well; three infected eyes were completely normal by the ninth week and the remaining three infected eyes were functionally good organs. By the 13th week four eyes were completely normal and the remaining two had minimal lesions of no great significance. It will be noted that of these six animals

TABLE II

Subconjunctival Injection of 1,000,000 *Units Penicillin in* 1 *ml. Water*

Infection: Intravitreal injection of 250,000 organisms *Staph. aureus* 663

Rabbit No.	At 4 days	At 24 days	At 9 weeks	At 13 weeks
Treatment at 3 *hours and* 24 *hours after infection*				
1	Hypopyon, eye quiet, but shows grey reflex	Destroyed on 10th day	—	—
2	Cornea hazy	Dense central corneal opacity, good red reflex	Slight corneal haze, vitreous clear, penicillin retinitis	Very slight corneal opacity and penicillin retinitis
3	Leucoma, otherwise normal	Small corneal opacity, vitreous clear, small area of organization in periphery of vitreous below	Slight corneal scar, penicillin retinitis	Normal
4	Died on 3rd day	—	—	—
5	Heavy conjunctivitis, cornea hazy	Corneal opacity, good red reflex, vitreous probably normal	Normal	Normal
6	Upper third of cornea hazy	Small corneal opacity, fairly heavy central vitreous opacity, penicillin retinitis	Normal	Normal
Treatment at 3 *hours,* 24 *hours, and* 48 *hours after infection*				
7	Upper cornea hazy	Cornea clear, central vitreous opacity	Normal	Small postcortical lens opacity
8	Eye normal, but conjunctiva inflamed	Cornea and vitreous clear, penicillin retinitis	Slight penicillin retinitis	Normal
9	Cornea hazy	Destroyed on 10th day	—	—
10	Cornea hazy	Destroyed on 10th day	—	—
11	Cornea opaque	Destroyed on 10th day	—	—
12	Cornea opaque	Destroyed on 10th day	—	—

treated to conclusion four had received only two injections, one at 3 hours and the other at 24 hours after infection.

(*b*) As these results were inconclusive a further batch of eight rabbits was infected and six were treated at 3 and 24 hours, the remaining two being kept as controls. The controls developed panophthalmitis within 36 hours and were destroyed. The results obtained in the treated animals are set out in Table III. It will be seen that in no case was there a complete recovery, and that in only two cases could the result be regarded as reasonably satisfactory.

TABLE III

Subconjunctival Injection of 1,000,000 *Units Penicillin in* 1 *ml. Water*

Infection: Intravitreal injection of 250,000 organisms *Staph. aureus* 663

Treatment at 3 *hours and* 24 *hours after infection*

Rabbit No.	At 10 days	At 5 weeks	At 8 weeks
13	Some corneal haze, vitreous clear, localized opacity of retina below (? needle injury)	Slight corneal haze above, penicillin retinitis, good functioning eye	Vitreous opacity in needle track, good functioning eye
14	Cornea clear, vitreous organized	Organized vitreous, use-eye	No change
15	Extensive corneal reaction, upper part of vitreous organized	Died, but eye condition apparently satisfactory	—
16	Cornea clear, vitreous opacities. (? good functioning eye)	Steel-grey organized vitreous	No change
17	Vitreous hazy, two white organized opacities	Traumatic detachment of retina	No change
18	Cornea normal, fairly dense vitreous opacities with one organized opacity	Needle track in vitreous with surrounding opacities, fairly good functioning eye	Vitreous opacities above, penicillin retinitis below, fairly good functioning eye

(*c*) On the assumption that a less virulent infection might give more consistent results a further batch of ten rabbits was infected with 100,000 organisms. Into two of these, dead organisms (heat-killed) were injected, and two further rabbits injected with living organisms were used as controls. The controls ran their usual destructive course, and the two rabbits which had received dead organisms showed no tangible reaction—in one case the eye was completely normal 7 days later, and in the other there was a

circumscribed vitreous opacity in the track of the injecting needle. The results in the remaining six treated at 3 and 24 hours, are set out in Table IV. It will be seen that here again no complete recovery is recorded, but that in two eyes the result could be regarded as reasonably satisfactory.

TABLE IV

Subconjunctival Injection of 1,000,000 *Units Penicillin in* 1 *ml. Water*

Infection: Intravitreal injection of 100,000 organisms *Staph. aureus* 663

Treatment at 3 *hours and* 24 *hours after infection*

Rabbit No.	At 7 days	At 28 days
19	Localized corneal vitreous opacities, functioning eye, fundus normal	Localized vitreous opacity, good functioning eye
20	Vitreous haze, fundus just visible	Eye grossly infected (relapse one week previously)
21	Vitreous haze, fundus just visible	Slight penicillin retinopathy, otherwise normal
22	Marked iritis, occluded pupil	Eye grossly inflamed and useless, cornea opaque
21	Organized vitreous	Eye grossly inflamed and useless, cornea opaque
22	Vitreous haze with some organization	Organized vitreous, some inflammation

Treatment of Less Severe Infection by Subconjunctival Injection of 250,000 Units.—In these cases the inconclusive results suggested two possibilities. In the first place, there was the possibility that the heavy infection by 250,000 or 100,000 organisms was in itself a limiting factor in obtaining adequate results. The second and more likely possibility was that, unlike human patients, rabbits do not tolerate subconjunctival injection of 1,000,000 units. It was observed repeatedly that the rabbits tended to scratch their eyes and it was felt that much of the reaction seen in these experimental eyes was the result of reinfection of mechanical injury. In the last series of experiments the infecting dose was therefore reduced to 50,000 organisms and the therapeutic dose to 250,000 units. The first treatment was given a quarter of an hour after infection and the second 24 hours after infection. Two rabbits were used as controls and developed panophthalmitis within 24 hours. To prevent them from scratching their eyes with their claws, all animals were fitted with cardboard collars which were removed after 48 hours.

The results in ten treated animals are shown in Table V, from which it can be seen that three of the ten experimental eyes were completely normal at six days and that no substantial lesion was present in any of the remainder. Three days later, one of the animals had died and of the remaining nine only two had minor corneal lesions. At 17 days, one eye showed considerable vitreous disturbances and the rest could be regarded as satisfactory. At

TABLE V

Subconjunctival Injection of 250,000 *Units Penicillin in* 0.5 *ml. Adrenaline*

Infection: Intravitreal injection of 50,000 organisms *Staph. aureus* 663

Treatment at ½ hour and 24 hours after infection

Rabbit No.	At 6 days	At 9 days	At 17 days	At 34 days
23	Eye normal	Normal	Normal	Normal
24	Eye normal	Normal	Normal	Normal
25	Eye normal	Normal	Large vitreous opacity above, inflammatory mass below, functioning eye	Infection flared up, animal killed, eye shows panophthalmitis
26	Slight conjunctival re-action	Normal	Some organized vitreous opacities, functioning eye	Normal
27	Cornea hazy, red reflex	Corneal haze less	Normal	Normal
28	Cornea hazy, conjunctiva swollen, good red reflex	Corneal haze less	Normal	Normal
29	Conjunctiva swollen, good red reflex	Normal	Normal	Normal
30	Normal	Normal	Normal	Normal
31	Found dead, eye excised and found normal	—	—	—
32	Upper lids swollen, good red reflex	Normal	Normal	Normal

34 days, all but one eye were normal and the eye that at 17 days had shown vitreous disturbances was now definitely grossly infected and at post-mortem examination showed extensive panophthalmitis. As the animal that had died on the 6th day had shown histologically a normal eye, the results of this series

may be taken as nine complete recoveries in ten infected eyes. In four of the nine eyes that were fully recovered, the track of the infecting needle could be seen in the vitreous.

It should be noted that in this experiment treatment was begun within a quarter of an hour of infection and maintained by a second injection of 250,000 units penicillin in 0·5 ml. adrenaline.

Discussion

In the light of the findings recorded in Table V, two things are clear.

(1) Vitreous infection can be controlled adequately by subconjunctival injection of penicillin.
(2) In the experimental animal results are limited by the amount of penicillin given and by the time within which treatment is instituted.

It is impossible to apply experimental findings uncritically to clinical conditions. An experimental animal with an infecting dose of either 250,000, 100,000, or 50,000 organisms has obviously no close parallel to clinical infections. What is of significance clinically, is that with an infecting dose of 50,000 organisms panophthalmitis develops within 48 hours in the experimental animal. It is therefore likely that most clinical infections are initially far less severe. It is also of relevance clinically that experimental infections of this type can be fully controlled by subconjunctival injections of penicillin, if the nine successful results out of ten recorded in Table V may be taken as evidence. In man injections of 1,000,000 units in 1 ml. solvent are relatively well tolerated. This does not apply to the rabbit, so that if any deductions may be drawn from these observations the prospects of controlling vitreous infection clinically are as good as these experimental results suggest.

The time factor is all-important. Nothing can be expected from a vitreous that already consists of a collection of pus. How soon such a condition develops in man will obviously depend on the virulence of the organism and possibly on the number of organisms introduced initially. In all cases it is obvious that treatment must begin early and that the classical sign of vitreous infection — a yellow vitreous reflex — is not an indication for treatment but evidence that the eye is already beyond treatment.

On the basis of the results recorded here the following clinical procedure is suggested:

(1) Treatment should be instituted at the earliest possible moment when infection of the vitreous is suspected or may become a possibility.
(2) Such treatment should be energetic and maintained beyond the point when all danger is past. It consists of giving 1,000,000 units crystalline penicillin

dissolved in 1 ml. water and 5 minims adrenaline 1:1,000. The injection should be repeated after 24 hours and maintained at the same interval for some two or three days after the vitreous is completely clear. In most cases this will mean maintaining treatment for 5 to 7 days.

(3) Nothing is to be gained by giving smaller doses, and the intravitreal injection of penicillin is clearly neither so desirable nor so effective as subconjunctival injection.

Summary

(1) Experimental infection of the vitreous by 50,000 organisms *Staph. aureus 663* leads to panophthalmitis within 48 hours.

(2) In nine out of ten experimental eyes, complete recovery was obtained by subconjunctival injection of 250,000 units crystalline penicillin in 0·5 ml. adrenaline 1:1,000 injected subconjunctivally at ¼ hour and 24 hours after infection. In the one eye that ended with panophthalmitis there was initial control with subsequent relapse.

(3) Heavier infections and heavier doses of penicillin gave inconsistent results, partly because the rabbit does not tolerate large subconjunctival doses of penicillin.

We are indebted to Mr. B. Helliwell and Mrs. I. Moncrieff of the Research Division, Glaxo Laboratories, for technical assistance.

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THERAPEUTIC ACTION OF A PITUITARY EXTRACT IN RETINITIS PIGMENTOSA*

BY

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ONE of the theories put forward to explain retinitis pigmentosa attributes this condition to endocrine disorders. Several authors, among them Bardet (1919) and Bing (1931), have suggested that the adiposo-genital dystrophy seen in the Laurence-Moon-Biedl syndrome is of hypophyseal origin; the first to state that the disease as a whole was due to a diencephalic lesion was Sterling (1930). Zondek and Koehler (1932) maintained that ordinary retinitis pigmentosa, as well as that observed in the Laurence-Moon-Biedl syndrome, was due to hypophyso-tuberal changes. These theories have led to the trial of total pituitary extracts in the treatment of retinitis pigmentosa. With this medication, Reilly and Lisser (1932) obtained a favourable effect upon the visual acuity of a patient with the Laurence-Moon-Biedl syndrome. Viallefont (1936) found improvement in visual acuity and hemeralopia in three cases of retinitis pigmentosa. Pesme and Hirtz (1937), treating a case of Laurence-Moon-Biedl syndrome in this manner, obtained an improvement in vision with a decrease in photophobia and nystagmus. Jores (1933), instilling melanotropic hormone into only one eye, in man, found an increased rate of dark adaptation in that eye. This led Basile (1939) to use a pituitary extract containing this hormone in the treatment of retinitis pigmentosa; he used it in subconjunctival and subcutaneous injections and in instillations, and obtained an improvement in the hemeralopia in several cases of retinitis pigmentosa, but not in visual acuity. Gonzalez Vanrell and others (1948; 1949) also obtained an evident improvement in visual acuity in this disease by the use of subcutaneous injections of an extract containing melanotropic hormone. Later, Mussio-Fournier and others (1949) obtained favourable results in retinitis pigmentosa with conjunctival instillations of an extract having a high content of melanotropic hormone.

* Received for publication May 11, 1950.

Treatment

The extract used is prepared from intermediate and posterior lobes of bovine hypophyses; it has no oxytocic or vasopressor effect, but has an intense melanotropic action. It is used both in the form of subcutaneous injections and in ocular instillations. The injectable extract contains 400 frog units per ml. and is generally given in twice weekly injections of 1 ml. The extract prepared for instillation contains 16,000 U. per ml.; it has a similar *p*H to that of the lacrimal secretion, and is more or less isotonic therewith. We have generally made two instillations per week, but the frequency depends upon the results obtained. Thus, in some cases, the favourable effect of each instillation only lasts two or three days, while in others we have seen it extend to 15 or 20 days or even two months. Three drops are instilled into each eye at 5′ intervals between drops, and 30′ to 60′ after the last drop the effect upon the vision is checked. In the majority of cases with favourable results, these appear within this time.

The histories of 22 cases treated with pituitary extract are given below.

Case Histories*

Case 1.—S.S., male, aged 23 years, seen in March, 1947. Typical retinitis pigmentosa with posterior capsulo-lenticular opacities. Visual acuity: R.E., 0·2; L.E., 0·4. Visual field showing a concentric constriction close to the fixation point. Treatment was begun with injections of extract and three months later vision was 0·7 in the right eye and 0·4 in the left. Hemeralopia and photophobia had decreased and headache, which had long been present, disappeared. By February, 1948, vision reached R.E. 0·9 and L.E. 0·7. Treatment has been continued regularly since then except for an absence of patient from city lasting 45 days, at the end of which vision had fallen to R.E. 0·7 and L.E. 0·5. One hour after instillation former values were recovered. On March 17, 1949, vision was: R.E., unity; L.E., 0·8. There were no fundus or field changes.

Case 2.—M.G., male, aged 28 years. Seen March, 1947. Typical retinitis pigmentosa. Vision: 0·5 in both eyes. Astigmatism, correction of which does not increase vision. Visual field: ring scotoma from 10° to 30°. Treatment with injections was begun, and on July 4, 1947, visual acuity was R.E. 0·9 and L.E. 0·7. Hemeralopia and photophobia had decreased. On October 30, 1947, vision was 0·9 in each eye. Patient has been lost sight of since then.

Case 3.—B.R., male, aged 54 years. Seen February, 1947. R.E. with typical retinitis pigmentosa. L.E. long since enucleated. Vision without correction: R.E. counts fingers at 30 cms. Lenticular opacities. In March, 1947, treatment was begun with subcutaneous injections, twice weekly, of the pituitary extract. On July 4, 1947, vision was 0·2. Patient was now able to go about the streets alone. Treatment was continued and in April, 1950, vision was 0·6. Hemeralopia and photophobia improved. No improvement in visual field.

Case 4.—J.B., male, aged 48 years. Seen June, 1947. Retinitis pigmentosa. Vision: R.E. 0·04; L.E. 0·02. Treated with injections. On November 17, 1947, vision was: R.E. 0·1 and L.E. 0·04. Patient during this time did not follow treatment regularly and was lost sight of after the date mentioned.

* Visual acuity is given according to the International Decimal Scale.

Case 5.—A.S.B., female, aged 37 years. Seen June, 1948. Retinitis pigmentosa. Vision: R.E. 0·5; L.E. 0·3. Visual fields constricted to within 10°-15° of fixation point. Two injections were given per week, and after the twentieth injection vision reached unity. The hemeralopia improved. Visual fields remained the same.

Case 6.—V.A., male, aged 49 years. Seen April, 1948. Retinitis pigmentosa. Vision: 0·6 in both eyes. Slight lenticular opacities of congenital appearance. Signs of sclerosis in the arteries of the fundi, consistent with hypertension. Visual fields constricted to 10° of fixation point. After 20 injections vision became normal. Hemeralopia improved. From October, 1948, until July 31, 1949, treatment was continued with one injection per week, the improvement persisting.

Case 7.—F.P.F., male, aged 56 years. Seen November 17, 1948. Retinitis pigmentosa. Advanced sclerosis of both lenses. Chronic simple glaucoma. Vision: R.E. 0·25; L.E. 0·25. Visual fields constricted to 5°-7° of fixation point. With injections and four instillations vision reached 0·5 in both eyes on January 5, 1949. In the right eye visual field increased 5° on some meridians.

Case 8.—P.D., male, aged 54 years. Seen on November 12, 1948. Retinitis pigmentosa. Vision with correction: 0·5 in both eyes. Fields reduced to within 5° of fixation point. On this date, after an instillation, vision reached 0·7 in both eyes. Instillations were continued and on December 21, 1948, corrected vision reached 0·9 in both eyes. In February, 1949, fields had increased 3° on some meridians. Hemeralopia improved. An improvement is obtained in the photophobia, but only lasting 24 hours after each instillation. Treatment was continued and on July 20, 1949, improvement persisted.

Case 9.—M.F.C., female, aged 61 years. Seen November, 1948. Retinitis pigmentosa. Vision: R.E. 0·3; L.E. 0·15. Fields constricted to within 2°-4° of fixation point. On April 20, 1949, after a series of 40 injections and 4 instillations, vision was 0·5 (doubtful) in both eyes. Hemeralopia had improved. Fields unchanged.

Case 10.—H.F.I., female, aged 58 years. Seen November 17, 1948. Retinitis pigmentosa. Chronic simple glaucoma and advanced opacity of both lenses. Vision: R.E. 0·3; L.E. 0·15. Superior fields narrowed to within 6° or 8° of fixation point; inferior fields to within 18° or 22°. On April 20, 1949, after 40 injections and 4 instillations, vision was 0·5 in both eyes. Fields had increased as much as 4° on some meridians. Hemeralopia had not improved.

Case 11.—M.D.T., female, aged 38 years. Seen January 18, 1949. Vision: 0·5 in both eyes. Fields constricted to within 2° of fixation point. On February 1, 1949, after 6 injections vision was 0·6 in both eyes. On March 9, 1949, nasal and temporal fields had increased 3° in both eyes. There was no improvement of the hemeralopia.

Case 12.—J.D.C., male, aged 36 years. Seen December 1, 1948. Typical retinis pigmentosa. Vision: R.E. 0·3; L.E. 0·5. Fields: R.E. constricted to within 5° of fixation point, concentrically; L.E. the same, but extending to 9° upon the temporal side of field only. After 18 injections vision was 0·6 in both eyes. By April, 1949, fields were of 10° extending to 13° on both nasal and temporal sides. Improvement in both hemeralopia and photophobia.

Case 13.—R.B.H., female, aged 45 years. Seen November, 1948. Typical retinitis pigmentosa. Vision: R.E. 0·25; L.E. 0·3. Fields constricted in both eyes: R.E., nasal field reduced to 2° and temporal to 5° of fixation point; L.E., nasal field reduced to 2° and temporal field to 4°. In January, 1949, after treatment, vision was 0·6 in both eyes, and fields were both circular as follows: R.E. 5° and L.E. 4°. Improvement was observed in both hemeralopia and photophobia.

Case 14.—A.V., male, aged 58 years. Seen October 4, 1948. Typical retinitis pigmentosa. Slight posterior opacities in both lenses. Hemeralopia. Photophobia. Vision: R.E. 0·5; L.E. 0·1; peripheral vision only, due to destructive lesion of the macula of the latter eye. Fields 10° to 15° from fixation point. After 15 injections vision in R.E. increased to 0·6; L.E. did not improve. After 40 injections vision unchanged. Hemeralopia no better. Photophobia decreased.

Case 15.—A.B., male, aged 47 years. Seen October 5, 1948. Retinitis pigmentosa. Vision: R.E. 0·4; L.E. fingers at 30 cms. Slight lenticular opacities. Field constricted almost to fixation point. Treatment was started with injections, and after one month vision was: R.E. 0·7 and L.E. 0·04. Hemeralopia and photophobia

distinctly improved. On November 5 an instillation was made and 30′ later vision was: R.E. 0·9 and L.E. 0·1. Treatment was continued with injections, and in March, 1949, improvement in vision persisted. Improvement of hemeralopia and photophobia, fields unchanged. Reading improved, so much so that patient who could previously only read a few paragraphs at a time, is now able to read a whole page of a newspaper.

Case 16.—L.B.F., female, aged 50 years. Seen September 21, 1948. Retinitis pigmentosa. Vision: 0·6 in both eyes. Hemeralopia and photophobia. Fields constricted to within 10° of fixation point. Two injections were given per week, and after the fifth injection vision was 0·8 in both eyes. Hemeralopia and photophobia improved. Injections were continued and on November 8 vision was still 0·8 in both eyes. On this date an instillation was made and 30′ later vision reached unity in both eyes. Hemeralopia had decreased so considerably that patient was able to go out alone at night, which she had not been able to do for five years. A combined treatment was continued with, and on July 28, 1949, the improvement persisted without field changes.

Case 17.—A.P.Q., female, aged 44 years. Seen in October, 1948. Retinitis pigmentosa. Vision: R.E. 0·6; L.E. 0·02. Hemeralopia. Fields constricted to fixation point. Treated with injections from the first day. On November 5, 1948, vision was: R.E. 0·9; L.E. 0·1. Hemeralopia improved. Since then patient has not returned for observation.

Case 18.—T.S., male, aged 28 years. Seen February 24, 1949. Retinitis pigmentosa. Vision: 0·6 in both eyes. Fields constricted to within 5° and 10° of fixation point. Forty minutes after instillation vision increased to 0·9 in both eyes. On March 12, after having received two injections, these same values were found. After this, four more instillations were made, and on April 6 visual acuity reached unity in both eyes. Hemeralopia improved.

Case 19.—O.L., male, aged 42 years. Seen January 20, 1949. Retinitis pigmentosa. Vision: R.E. 0·04; L.E. 0·1. Fields constricted to within 2° of fixation point. Combined treatment was given with both injections and instillations, without evident effects.

Case 20.—A.P., male, aged 25 years. Seen December 29, 1948. Retinitis pigmentosa. Vision: Finger movements at 30 cms. On March 4, 1949, after a combined treatment with subcutaneous injections and instillations, vision was: R.E. 0·04; L.E. counted fingers at one metre. On March 21 a retrobulbar injection of 0·5 ml. extract was made into the right eye. One hour later vision in that eye was 0·1 at a distance of 4 metres. From then until May 9 patient received two subcutaneous injections per week, and states that for the first time for a year he is able to go about the city unaccompanied, although with some difficulty. Excentric vision is now 0·1 in R.E. and there have been no further changes in L.E.

Case 21.—M.P., male, aged 29 years. Seen March 29, 1949. Retinitis pigmentosa. Vision: R.E. 0·02; L.E. 0·04. Posterior lenticular opacities in both eyes. On April 28, 1949, after 8 instillations, there was no improvement.

Case 22.—P.V., male, aged 35 years. Seen April 11, 1949. Retinitis pigmentosa. Vision: R.E. unity; L.E. 0·6. Fields in the neighbourhood of 30°. On April 28, after two instillations, vision was unity in both eyes. Photophobia diminished. Before treatment was started, patient suffered from headache after reading or writing for two hours. This trouble has now disappeared.

Results

Out of a total of 22 patients treated, the results were favourable (as regards visual acuity) in sixteen (Cases 1, 2, 3, 5, 6, 7, 8, 10, 12, 13, 15, 16, 17, 18, 20, 22), negative in two (19 and 21), and doubtful in four (4, 9, 11, and 14).

Increase in vision has been as great as 0·8 (Case 1); it has been observed in patients with lenticular opacities of varying degree (Cases 1, 3, 6, 7, and 10), including two cases of simple glaucoma (6 and 10). Hemeralopia improved in fourteen cases (1, 2, 3, 4, 5,

6, 7, 8, 12, 13, 15, 16, 17, and 18); there was no improvement in seven, and of the remainder there are no data available. Out of thirteen patients with photophobia, ten improved.

The visual field was only studied in fourteen cases during treatment: in eight the field did not vary, while in six there were small increases of 2° to 5°, in some cases concentrical and in others segmental. We believe that further observations will be necessary to decide upon the significance of these apparent increases in visual fields.

The increase in visual acuity was obtained in some cases with injections (Cases 1, 2, 3, 5, 7, 12, 13, 14, 17, and 20), in others with instillations (8 and 22), and in others again with a combined treatment (6, 10, 15, and 16).

Of the three methods of administration of the extract (subcutaneous injection, instillation, and a combination of the two) we consider instillation to be the best. Thus, in two cases (15 and 16) after obtaining considerable improvement with a series of injections extending over several weeks, vision increased 0·2 in each case, 30′ after a single instillation. This efficacy combined with its simplicity makes instillation the ideal method.

As regards the duration of the improvement, our information is limited by the short time during which we have been using this medication. However, in our first patient treated (Case 3) the improvement has increased steadily for the last three years; the patient began with vision counting fingers, and now has vision 0·6.

In those cases in which no result is obtained by our methods, it is suggested that a trial be made with subconjunctival and retrobulbar injections.

Discussion

In the first place we wish to point out that the success obtained in the treatment of retinitis pigmentosa with a pituitary extract in no way confirms the diencephalo-hypophyseal origin of this disease, inasmuch as this medication has been seen by us to give similar therapeutic results in the visual disorders of albinism and retinitis diabetica (Mussio-Fournier and others, 1949b, d, e), in high myopia (Conti and others, 1949), in hypertensive retinopathy, and in senile degeneration of the macula (Mussio-Fournier and others, 1949c)*.

As to the question of how the preparation employed reaches the retina, little can be said. However, since the application of

* Velter and others (1950) and Dollfus (1950) obtained favourable results in France with our pituitary extract, and similar results have been reported in Argentina by P. O. Cuzzani (1949) and B. Malamud (1949).

the preparation to one eye favourably affected both, absorption and transportation by the blood would seem to be likely.

The third point to consider is the mechanism by which the substance acts. No doubt there is an action on the retina. The improvement of the hemeralopia, a disorder due to an alteration of the rods, indicates that the medication acts upon the latter. The increase in visual acuity observed is most likely due to an effect upon the cones*. Just as digitalis is beneficial in cardiac insufficiency, whatever the cause may be, so this extract increases the functional capacity of the retina in disorders of widely differing aetiology.

Throughout our researches we have borne in mind two hypotheses: first that the extract operates through a physiological action of the melanotropic hormone upon the vision; second that it acts through a non-hormonal pharmacological property.

The therapeutic success obtained by us latterly with instillations of an extract of muscle tissue in various disorders of the eye (retinitis pigmentosa, high myopia, diabetic retinopathy) seems to confirm the second hypothesis (Mussio-Fournier and others, 1949c).

Finally, it is to be remembered that Filatov, using implants and extracts of widely differing tissues, states he has obtained good results in various diseases of the eyes. We do not consider ourselves to be in a position to say, as yet, whether or not the active substance in our extract is the same as Filatov's "biogenic substances", but we wish to call attention to the simplicity of our instillation technique. As this treatment is not aetiologic but merely symptomatic, it would seem reasonable to suppose that the diseases of the eye thus treated will themselves continue their habitual chronic course. The exact percentage of improvement and average duration will only be obtained after further research.

Summary

Twenty-two cases of retinitis pigmentosa were treated with a pituitary extract, favourable results being obtained in sixteen. The mode of action of the extract is discussed, although it is not known what the active principle may be.

We are indebted to Laboratorios Senac, Montevideo, Uruguay, for their collaboration in preparing the extracts used in this research.

* The instillations of normal saline solution into the conjunctiva of several patients produced no effect, favourable results being obtained when pituitary extract was afterwards instilled, thus showing that this treatment does not act through psychotherapy.

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RECESSIVE SEX-LINKED INHERITANCE OF EXTERNAL OPHTHALMOPLEGIA AND MYOPIA COINCIDENT WITH OTHER DYSPLASIAS*

BY

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DIFFERENT authors have reported several cases of congenital external ophthalmoplegia, some of which were myopic. No one, however, has paid special attention to this occurrence. Familial external ophthalmoplegia has been reported as inherited in two forms: dominant and recessive.

The fact that all our cases with ophthalmoplegia were myopic, the special form of transmission of the pathological gene, and the presence of a number of stigmata in the affected subjects and in the carriers of the pathological gene, are the most interesting features of our communication.

The ophthalmological picture of our four patients is strikingly similar in all (Fig. 1). They present the following characteristics:

(1) Complete bilateral ptosis.
(2) Almost complete, or complete, bilateral external ophthalmoplegia. Slight lateral movements are obtainable in some of them, but they are scarce and do not reach 20°.
(3) Divergent squint is present in three cases (III, 4; III, 6; IV, 5), and convergent squint in the other (IV, 6).
(4) The pupils are eccentric, dyscoric, and anisocoric. The light reflex is normal in seven eyes and absent in the eighth. The accommodative reflex is very difficult to obtain because of the lack of convergence and the existence of high myopia.
(5) Myopia of high degree in the three older patients and of slight degree in the youngest; fairly good visual acuity without glasses (because of the stenopeic slit produced by the ptosis) only very slightly improved by their use.
(6) Myopic fundus alterations (staphylomata and Foerster-Fuchs macular spot).

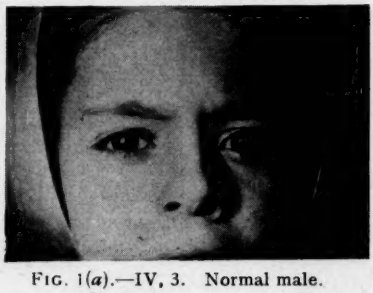
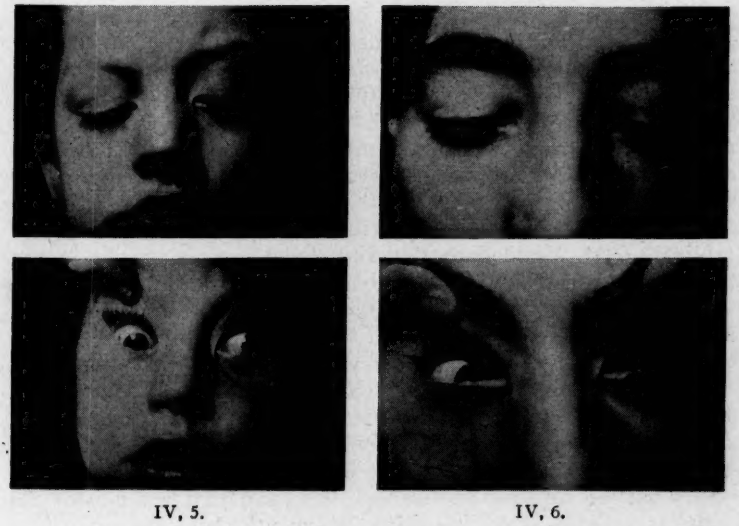


FIG. 1(*a*).—IV, 3. Normal male.

Of the living male subjects, only one (IV, 3) has normal eyes (Fig. 1*a*); two other afflicted males died, one in early childhood (IV, 7), the other at the age of 46 years. (Generation II). The genealogical tree (Fig. 2, p. 664) shows that most of the men are phenotypically affected, and that all the women are phenotypically

* Received for publication July 7, 1950.

III, 4. III, 6.



IV, 5. IV, 6.

FIG. 1.—Four afflicted male members of the family.

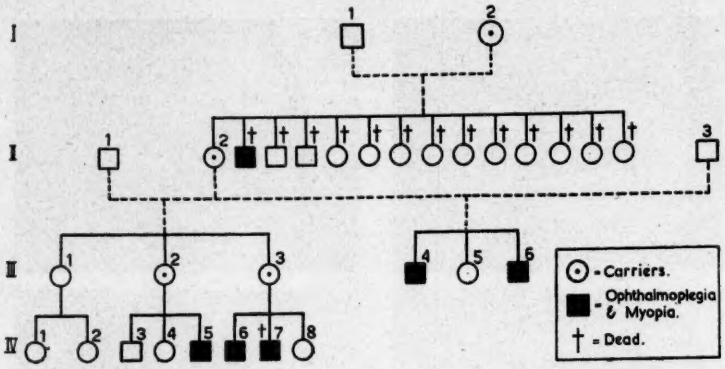


FIG. 2.—Recessive sex-linked pedigree of external ophthalmoplegia and myopia.

healthy. Some of the women are genotypically affected and therefore transmit the gene. The inheritance of this gene in this family is recessive and sex-linked. As far as we have been able to discover in the literature there is no earlier reference to inheritance of this type for this particular disease.

The clinical and neurological examination carried out by one of us (J. C. O. de Z.) on all fourteen living members of the family, enabled us to detect a number of signs enumerated in Fig. 3 (opposite). As may be observed, the stigmata are apparent only in the affected males and in the female transmitters of the pathological gene. The most interesting symptom is the absence of knee and ankle jerks. From the presence or absence of these reflexes in the women of this family, we have been able to point out which persons are transmitters of the pathological gene and which are not.

This point is of great practical interest because, basing our replies on the Mendelian laws and the degree of purity in the pedigree, we can say which members of the family may, and which may not, have issue without danger of bringing more afflicted children into the world. Thus the family may survive through its fittest members, for we shall be able to assure the homozygotes that their descendants will be born completely healthy. We can advise the heterozygotic women that half of their descendants will be born afflicted or as transmitters of this disease. Afflicted males can be told that all their male descendants will be healthy non-transmitters, and that a study of the patellar reflexes will determine which of their daughters are transmitters of the ophthalmoplegic gene.

NAME	1	2	3	4	5			6	7	8	9	10
					a	b	c					
E. L. d. D. y F. ⊙	−	±	+	−	−	−	−	?	+	−	+	−
E. d. P. ⊙	−	−	±	−	−	−	±	?	−	−	+	+
E. N. ⊙	−	−	+	+	−	−	+	−	−	−	+	−
A. M. ⊙	−	−	+	−				?	−	+	+	−
N. D. ○	−	−	+	−	+	−	+	?	+	−	+	−
N. de P. ○	−	−	−	−	−	−	+	−	−	−	−	−
J. M. de P. ○	−	−	−	−	−	−	−	−	−	±	−	−
N. E. N. ○	−	−	−	−	−	−	−	−	−	−	−	−
M. C. M. ○	−	−	−	−	−	−	−	−	−	−	−	−
P. V. ■†	+											
A. D. ■	+	+	+	+	−	−	+	+	+	−	−	+
A. D. ■	+	+	+	+	+	+	+	+	+	+	−	+
N. O. N. □	−	−	−	+	−	−	−	−	−	−	−	−
O. N. ■	+	+	+	+	+	+	+	+	−	−	−	+
B. M. ■	+	+	+	−		+	+	?	−	+	−	+
M. ■†	+											

FIG. 3.—Ocular and extra-ocular signs in sixteen members of the family.

1. Ophthalmoplegia.
2. Myopia.
3. Absence of knee and ankle jerks.
4. Left-handedness.
5. Myelodysplasia { a–Enuresis. b–Spina bifida. c–Flat feet.
6. Cardiac malformation.
7. Hernia and varices.
8. Anomalous occlusion of the teeth.
9. Goitre.
10. Thoracic malformation.

All the members of this family are natives of Argentina, and it is impossible to investigate retrospectively the exact moment that the mutation or translocation of the gene from an autosome to the unpaired part of the X chromosome occurred. It is to be remembered that this gene is recessive, and that in an autosome if the unions were not consanguineous it could have remained for many generations without manifesting itself. Because of the frequent illegal unions in this pedigree, it was impossible to trace any ancestors further than the first generation of the given tree. Every one of the signs evident in these patients could be accepted as dysrhaphic, but the absence of one (ophthalmoplegia) in the women, and its presence in the men, would prevent us from accepting all these stigmata as the result of one pleotropic gene.

The known position of the gene of hereditary sex-linked myopia in the non-homologous part of the X chromosome, the circumstance that all the affected members of this family are myopic, and the fact that a study of the literature reveals a marked

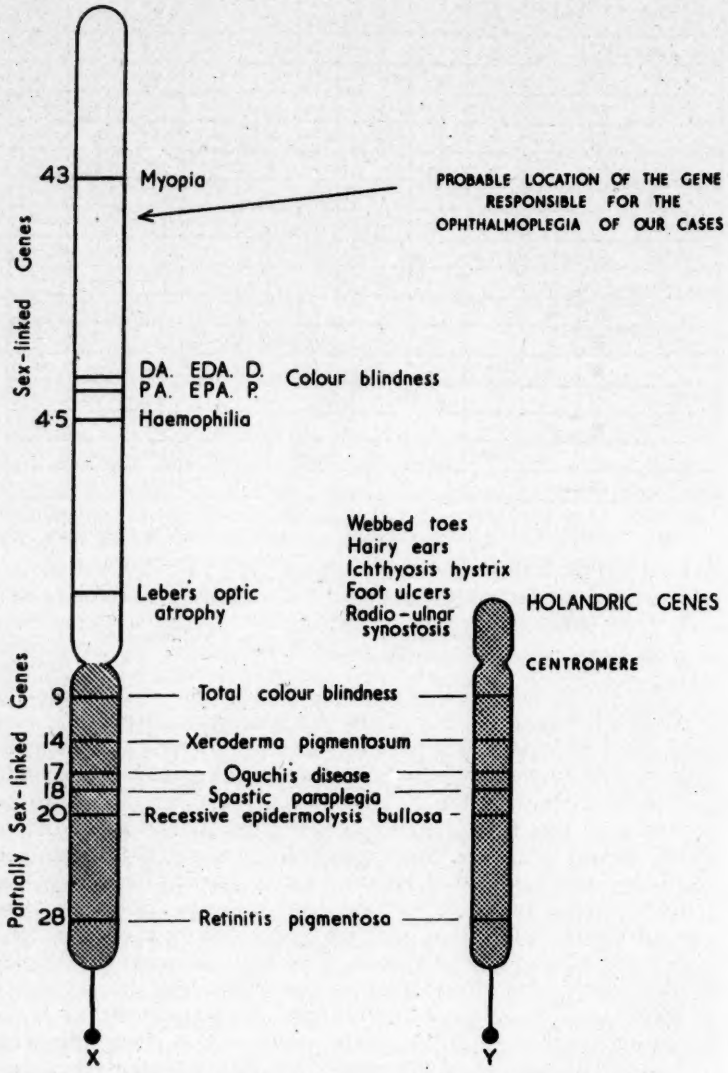


FIG. 4.—Diagram of the sex-chromosomes and some of their contained genes. (Courtesy of Macmillan, New York, and Gates, 1946.)

tendency for the co-existence of these two signs (ophthalmoplegia and myopia), suggest that the probable location of the pathological gene of our cases is close to that of the myopia. This location is shown in Fig. 4, adapted from Gates (1946).

Summary

A report is presented of a family with heriditary, sex-linked, congenital ophthalmoplegia. Six males out of seven had the disease. All the females were ophthalmologically normal. The coincidence of other signs (myopia, absence of tendon reflexes, etc.) suggests interesting conclusions.

This family is believed to be the first reported with this type of inheritance.

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CONTACT LENS IN UNILATERAL APHAKIA*

BY

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THE problem of uniocular cataract with good visual acuity in the other eye is an old, but by no means a solved, problem. The established view still upheld by many ophthalmologists, that such a cataract is best left alone, is based on the observation that the optical correction of unilateral aphakia is not satisfactory, as diplopia and general discomfort are experienced. Furthermore, the risks of the actual operation and of post-operative complications, the frequent occurrence of divergence, and the possible disappointment of the patient at the final result, foster this conservative attitude. Cowan (1949) states:

> The correction of monocular aphakia is impracticable, not only because of the diplopia due to aniseikonia and to the prismatic effect of the difference between the glasses, but also because the patient has two different optical instruments, one dynamic with more or less active accommodation and the other static.

It is generally agreed that (there being good visual acuity in the fellow eye) the correction of unilateral aphakia with spectacle lenses is disappointing, because of the aniseikonia and diplopia. In contradiction of this view, Kuhn and Kuhn (1949) advise normal spectacle lenses and report a series of 82 uniocular aphakias corrected in this way. Their results are startling: 83 per cent. of cases had no trouble whatsoever in wearing full correction; only 4 per cent. were totally unable to wear full correction; and the remaining 13 per cent. had moderate trouble for a few months. The patients were fitted with a temporary lens 4 to 6 weeks after the operation and an occluder was worn while the diplopia lasted. Although no details about binocular vision are given, they state that " some persons suppress one image but most of them actually have binocular vision. Hard as it is to understand ".

Most authors agree that a contact lens, at least theoretically, is the best remedy we have at present for abolishing the diplopia and aniseikonia which accompany the use of spectacle lenses. According to Town (1939), the diplopia is chiefly due to the prismatic effect of spectacle lenses of high positive power and not to aniseikonia, as is generally believed. The contact lens will abolish this prismatic effect, and the diplopia that may occur with a contact lens is probably due to muscle imbalance.

* Received for publication February 10, 1950.

The amount of aniseikonia in unilateral aphakias was calculated by Boeder (1938) to be about 25 per cent. This magnification is reduced by a contact lens to 11·4 per cent., and according to Blum and Babel (1948) is not more than 5 per cent. In order to equalize the two retinal images, Boeder suggested that the emmetropic (phakic) eye should be rendered 3D hypermetropic by a contact lens and that this should then be corrected with an ordinary spectacle lens. According to Blum this difference can also be abolished by an aniseikonic lens in an ordinary spectacle frame. The amount of aniseikonia that can be tolerated without impairment of binocular vision is not known exactly; Duke-Elder (1949) gives it as 5 per cent., above which binocular vision becomes difficult or impossible. On the other hand, according to Town (1939), the eye can achieve fusion with a difference in size of at least 10 to 20 per cent.

Contact lenses have been used extensively in uniocular aphakias for the past few years but the opinions of various authors differ in their evaluation; in a few cases good tolerance and restoration of binocular vision was attained (Town (1939) three cases; Girardet (1948) three cases; Maione (1949) three cases; Gettes and Ravdin (1949) one case), but others found contact lenses disappointing. Mann (1947), in an analysis of ten patients, found only one patient able to wear his contact lens with comfort; the rest complained of diplopia and discarded their lenses. Cross (1949), in a thorough survey of 875 contact lens wearers, found that 4 per cent. of these were fitted for uniocular aphakia, out of which only just over half were wearing them. His comment is interesting:

> *It was a surprise to realise that the percentage of aphakic persons wearing contact lenses were even less than the myopes. It appears that though a contact lens reduces the size of the image in the aphakic eye and overcomes the prismatic effect of a strong convex lens, this is not sufficient to allow fusion of images and comfortable vision in a very large proportion of cases. This is probably the result of absence of accommodation in the aphakic eye*

Present Investigation

In view of this divergence of opinion regarding the value of contact lenses in unilateral aphakia, it was decided to review all cases that have been fitted with a contact lens for this condition in one of the clinics at Moorfields Eye Hospital during the past 2 years. Since the aim was to restore binocular vision with the aid of a contact lens, all patients with poor visual acuity in the other eye were excluded from this series.

A short case history of eighteen consecutive patients in this series is given in the Table (pp. 670 and 671).

TABLE SHOWING RESULTS IN EIGHTEEN

Case No.	Sex	Age	Cataract		Complications (pre- or post-operative)	Duration of aphakia	Contact lens supplied
			Cause	Eye			
1	♀	22	I.O.F.B.	LE.		1945	November 1948
2	♂	54	Perforating corneal wound	LE.	Iris prolapse Corneal scarring	1947	March 1948
3	♂	19	Perforating corneal wound	LE.	Iris prolapse Corneal scarring Peripheral anterior synechiae	1945	January 1948
4	♂	13	Air-gun injury	RE.	Dislocated lens	1947	April 1948
5	♂	41	Perforating corneal wound	LE.	Iris prolapse Secondary glaucoma	1947	January 1948
6	♂	61	I.O.F.B.	RE.		1947	March 1948
7	♂	41	I.O.F.B.	RE.	Siderosis Vitreous prolapse	1948	November 1948
8	♂	60	Senility	RE.		1943	October 1948
9	♂	31	I.O.F.B.	LE.		1948	March 1949
10	♂	65	Senility	LE.	Choroid detachment Cystoid scarring	1948	January 1949
11	♂	23	I.O.F.B.	RE.		1948	January 1949
12	♀	66	Senility	LE.		1948	November 1948
13	♂	32	I.O.F.B.	RE.	Iris prolapse	1949	May 1949
14	♂	26	I.O.F.B.	RE.	Chorioretinal scarring	December 1949	January 1950
15	♂	48	Heterochromic cyclitis	LE.		November 1949	December 1949
16	♀	46	Not known	RE.		October 1949	December 1949
17	♀	48	Not known	RE.		1948	October 1949
18	♂	49	? Trauma	LE.		November 1949	December 1949

CONSECUTIVE CASES OF UNILATERAL APHAKIA

Visual acuity with contact lens		Binocular vision with contact lens		Orthoptic treatment	Tolerance of contact lens (hours)	Remarks
RE.	LE.	Single vision	Stereopsis			
6/5	6/9	yes	good	yes	4–6	Constant wear, comfortable
6/9	6/12	yes	good	yes	4	Constant wear, comfortable
6/5	6/9	yes	none	yes	5–6	Constant wear, comfortable
6/6	6/5	yes	good	yes	up to 18	Constant wear, comfortable
6/9	6/9	yes	good	no	4–5	Constant wear, comfortable
6/6	6/6	Weak fusion	none	yes	nil	Psychoneurotic symptoms
6/9	6/6	yes	good	yes	Does not wear it	Paresis of R. ext. rectus due to fractured skull
6/6	6/6	yes	good	no	5	Constant wear, comfortable
6/5	6/12	yes	good	yes	5–6	Constant wear, comfortable
6/6	6/9	yes	good	no	5	Constant wear, comfortable
6/5	6/5	yes	good	no	4	Constant wear, comfortable
6/9	6/12	yes	good	no	4	Constant wear, comfortable
6/6	6/6	yes	good	yes	8–9	Constant wear, comfortable
6/9	6/6	yes	good	yes	4–5	Constant wear, comfortable
6/5	6/9	yes	good	no	5	Constant wear, comfortable
6/9	6/6	yes	good	no	14	Constant wear, comfortable
6/9	6/6	yes	good	yes	14	Constant wear, comfortable
6/9	6/9	yes	good	no	5	Constant wear, comfortable Moderate myopia

It should be stated here, that certain cases were considered unlikely to benefit from contact lens and were rejected at the beginning. Manifest squints, considerable hyperphorias, amblyopias, nystagmus, central chorioretinal lesions, and chronic glaucoma were among the contraindications. This caution was necessary in view of the high cost of the contact lens.

The routine procedure was as follows: the patient was first refracted and the aphakic correction with spectacle lenses recorded. A trial contact lens was then inserted and the visual acuity ascertained. With this correction the fusion was tested and the muscle balance for distance measured; if the patient obtained immediate fusion, he was given a contact lens on loan and, where necessary, convergence exercises were carried out in the orthoptic department. As in most cases some degree of exophoria was present; this was treated during and after the contact-lens fittings. After the dispensing of the final contact lens, a +3DS was ordered for reading for the aphakic eye and, where necessary, a reading correction prescribed for the other eye. The contact lens used was of the Dallos type.

Most of the patients were thus examined and treated if necessary in the orthoptic department before ordering the permanent contact lens, as it was felt that the restoration of binocular vision was necessary before embarking on such a costly and time-consuming procedure. (No case needed more than six or eight orthoptic treatments.)

Discussion

Although the number of cases quoted is small, it demonstrates amply the value of contact lens in cases of uniocular aphakia. Of eighteen patients fitted with contact lens for this condition, sixteen have had binocular vision fully restored and are able to wear their contact lens constantly and with comfort. As one would expect, the majority (eleven patients) had traumatic cataract, and all except the two failures were able to resume their usual occupation. Seven of the traumatic cases had intra-ocular foreign bodies. Of the seven non-traumatic cataracts, six were of senile type and one was a complicated cataract due to heterochromic cyclitis.

The tolerance was good in all these cases; this may be due to the improved type of the contact lens or to reduced corneal sensitivity following the limbal section.

The age of the patients varied from 13 to 66 years and did not seem to influence the final result. Girardet (1948), however, believes that the best indication is in young adults with traumatic

cataract. He thinks that in older people the wearing of a contact lens requires a greater effort of tolerance and of manual dexterity, and he therefore advocates aniseikonic lenses instead. There seems to be no definite opinion regarding the time that should elapse between the cataract extraction and the fitting of the contact lens. Girardet is against an early fitting, though the logical step, if divergence be avoided, is to apply a corrective contact lens as soon as the limbal section is firmly healed and the eye shows no sign of irritation. In this series, this period varied, the shortest being 6 weeks from the cataract extraction.

Success in restoring binocular vision with a contact lens depends mainly, I believe, on the state of binocular vision existing before the onset of the trauma or disease that led to unilateral cataract. Assuming that good fusion was present and that the neuromuscular apparatus was not impaired by the trauma or disease, the ultimate result with a contact lens should be favourable.

Though there is no doubt that the absence of accommodation in the aphakic eye is an important obstacle in attaining comfortable binocular vision, the loss of accommodation alone cannot account for fusion failure, as Cowan (1949) and Cross (1949) believe. In a normal person the fusion amplitude remains unaltered if one eye is rendered cycloplegic and its total refraction fully corrected by a spectacle lens; I was able to verify this in cases where atropine had been used (as after corneal foreign bodies), and in cases of traumatic mydriasis with complete loss of accommodation.

The enthusiasm of the patient undergoing the tedious procedure of fitting, and his perseverence despite the initial discomfort and occasional diplopia, are other important and necessary factors.

The two failures in this series are instructive; in Case 6 there was an unmistakable neurotic element coupled with fear of loss of adequate compensation, and the fitting was undertaken in the hope that the contact lens might alleviate his complaints (neuralgic pain, inability to concentrate, etc.). In Case 7 the residual weakness of the external rectus muscle due to a previous trauma to the 6th nerve (fracture of skull), was not recognized before the fitting and, in spite of the presence of fusion and stereopsis, this muscular weakness proved a sufficient obstacle to comfortable binocular vision.

It appears, therefore, that considering the high cost of contact lenses, careful selection of cases is essential; patients with heterotropia, hyperphoria or amblyopia, or with neurotic

symptoms, are not likely to benefit from contact lenses. On the other hand, corneal scars, anterior peripheral synechiae, cystoid cicatrix, and slight vitreous prolapse, do not seem to be contra-indications, as all these conditions occurred in patients where full binocular vision was restored.

The necessity and value of orthoptic treatment cannot be too strongly stressed; it helps to improve the fusion amplitude and to reduce the exophoria that is usually present. Eight patients in this series did not require any orthoptic treatment at all, as their fusion was strong and no muscle imbalance was found. The majority, however, benefited greatly by the treatment, and my own belief is, that without orthoptic exercises, many cases would have been given up as failures.

In conclusion, contact lenses appear to offer us the best solution in the problem of the correction of uniocular aphakias; they are certainly superior to any other optical correction we have at present. The old *laissez-faire* attitude will no doubt change as more encouraging results appear in the literature and the selection of cases is more clearly defined.

Summary

(1) A short case history is given in tabular form, of eighteen consecutive patients with unilateral aphakia fitted with contact lens in the past two years, and the routine procedure outlined.

(2) Sixteen out of eighteen patients have had their binocular vision fully restored and are able to wear their contact lens in comfort.

(3) Stress is laid on the need for discrimination in selecting cases and on the value of orthoptic treatment in the re-education of binocular single vision.

I wish to express my thanks to Miss I. Mann for her encouragement, to Dr. J. Dallos for his valuable help and advice, and to the Misses Sheila and Beryl Mayou, who were responsible for the orthoptic treatment.

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AUREOMYCIN IN OPHTHALMOLOGY*

BY

D. AINSLIE

From the Ophthalmological Research Unit, Institute of Ophthalmology, London. Director of Research, Sir Stewart Duke-Elder

AUREOMYCIN has now become established as an important and powerful antibiotic and has proved itself effective in several ophthalmological infections which failed to respond to other treatment. A preliminary report has already been made from this clinic on the use of this drug in ophthalmology (Duke-Elder and others, 1950). The present communication describes our further experiences with this drug. In particular it has been found effective in resistant cases of conjunctivitis, blepharo-conjunctivitis, follicular conjunctivitis, and trachoma, and in some cases of keratitis and corneal ulceration.

The main disadvantage of aureomycin in ocular therapeutics is its poor penetration into the eye, whether given topically, subconjunctivally, or systemically. Experimental studies of the penetrability of aureomycin into the eye of the rabbit have been made by de Roetth (1949) and by Bellows and others (1950). Their results were similar. They found that a barely therapeutic level of aureomycin in the aqueous was obtained after a very large intravenous dosage (50mg./kg. bodyweight). Subconjunctival injection did not lead to a therapeutic level in the aqueous. Local administration of drops 0·5 per cent. to the conjunctival sac did not lead to any penetration in the intact eye. In cases of corneal ulceration or abrasion, however, aureomycin was found to penetrate into the cornea and aqueous. Theoretically intra-ocular injection is the only possible means of its introduction into the eye, but the direct injection of aureomycin into the anterior chamber is said to produce a severe iritis, which, however, gradually settles, whereas injection into the vitreous leads to retinal degeneration and fibrous tissue formation (Azzolini and Faldi, 1950; Pritikin and others, 1950).

Methods of Administration and Toxicity

In the series under review the four following methods of administration were employed:

(1) **Drops.**—0·5 per cent. aureomycin borate was used, administered at hourly intervals. In some cases of severe conjunctivitis

* Received for publication October 3, 1950.

in children the treatment was started by an intensive course, *i.e.*, one drop every minute for half an hour, one every five minutes for one hour, then hourly. No untoward effects were produced, there being no evidence of corneal damage or allergic response.

(2) **Ointment.**—In cases of blepharitis it was thought desirable to use an ointment. In addition it was necessary to find some preparation of aureomycin which remained stable for a considerable period. The fact that the drops deteriorated rapidly and were only effective for 24-48 hours, even if refrigerated, made outpatient administration difficult.

An anhydrous ointment was prepared, using 5 mg. aureomycin per gram of a eucerine base. This lasted for at least a month without appreciable loss of potency. A smoother ointment was prepared by first mixing the aureomycin with a very small amount of water, before adding to the eucerine. This latter ointment was still highly active after a week, but after three weeks its potency was reduced almost to nil. It was, however, less irritating to use.

In several cases a slight allergic response occurred as a result of the use of the anhydrous ointment. In one case the reaction was severe and necessitated cessation of treatment.

There is now a commercial preparation of aureomycin ointment 1 mg. per gram (Lederle). Only six tubes, obtained as samples, have been used, but it appears to be effective in this low concentration and no allergic response has been noted.

(3) **Systemic Administration.** — 500-750 mg. were given orally. Mild diarrhoea occurred in all cases. Nausea was common but actual vomiting only occurred in one case. In only one case was there a more severe toxic reaction, with vertigo and severe headache. The vertigo improved immediately the drug was stopped but the headache persisted for three weeks.

(4) **Sub-Conjunctival Administration.**—This method was used in three cases, 0·5 ml. of 0·5 per cent. aureomycin borate being given. Severe pain lasting for half an hour resulted, but there was no untoward reaction. In the case of a patient who had had six such injections, two days after the last one there was no chemosis, no scarring and only slight hyperaemia.

Clinical Applications

Conjunctivitis.—Eight cases of simple conjunctivitis were treated. All had had penicillin treatment, and three had had albucid and two oxycyanide of mercury in addition, without effect. All were left for two days without treatment and cultures taken. Five gave no growth on blood agar, although there was mucopurulent discharge at the time of taking the cultures. Three grew *Staph. aureus*, which was resistant to penicillin but sensitive to aureomycin (*in vitro*). All the

cases with "no growth" responded rapidly to aureomycin drops, being cured in from 3 to 10 days.

One particularly striking case was that of an infant, who had had two intensive courses of penicillin drops and in addition systemic penicillin therapy, all without effect. Four days of guttae aureomycin hourly eradicated the infection. At no time in this case was there any growth from cultures of the mucopurulent discharge.

Of the three cases apparently due to penicillin resistant *Staph. aureus* one cleared up rapidly and completely, but the remaining two recurred immediately treatment was stopped, even though systemic aureomycin was given and the lacrimal sacs were syringed.

Follicular Conjunctivitis.—Under this head are included thirteen cases of conjunctivitis characterized by the presence of small follicles of the palpebral conjunctivae and a thin mucopurulent discharge. In four cases there was a marginal ring of superficial corneal vascularization with small corneal ulcers. From three cases there was obtained a growth of *Staph. aureus*, but in the others cultures were sterile. Scrapings from the conjunctivae revealed inclusion bodies in five of the "sterile" cases.

Of ten cases which responded to aureomycin treatment, seven required only local treatment, but in three a cure was not effected until after a course of oral administration. Cures were effected in from 12 to 25 days. Of the three which were unsuccessful, two had had the condition for 2½ and 6½ years respectively and, although aureomycin, given intensively both locally and systemically, cleared up the condition, it recurred immediately treatment was stopped. Two out of the four cases with corneal vascularization responded.

Blepharitis.—Fourteen cases of long-standing blepharitis were treated. All had had numerous previous treatments. Cultures were taken in every case after at least 48 hours without treatment. In two cases there was no growth, but in eleven *Staph. aureus* (in nine cases insensitive to penicillin) was revealed. The remaining case grew penicillin-insensitive Friedländer bacillus.

The patients were all treated by aureomycin ointment given 2-hourly, and six received systemic therapy in addition. The results were most satisfactory, ten of the fourteen treated being clinically cured. In three cases the cure was effected only after a second course, and in one it was necessary to persist with treatment for over 6 weeks. The case in which culture showed Friedländer bacillus (and in which the blepharitis had been present for 6 years) cleared after 12 days' aureomycin ointment and did not recur.

Of the remaining four, two showed no response. Two improved but the infection was not eradicated and the condition recurred in spite of persistent treatment. All four unsuccessful cases had systemic administration in addition to local therapy. Only two out of the ten successful cases required systemic therapy.

One remarkable success occurred in a woman who had had blepharitis for 26 years and had had treatment with ung. hydrarg. ox. flav, ichthyol, ung. hyd. ammon. dil., lotio hyd. oxycyan., albucid, penicillin, and possibly other drugs. A good growth of *Staph. aureus*, slightly sensitive to penicillin but more so to aureomycin, was obtained. Twelve days' treatment with aureomycin ointment caused complete subsidence of the inflammation. Except for slight scarring of the lids causing irregularity of the hair follicles, nothing abnormal can be detected and there has been no recurrence during four months.

Trachoma.—It has been impossible in London to find entirely fresh cases of acute trachoma, but six cases of active trachoma have been treated. All showed pannus, follicles, and scarring. In five at least there was no doubt as to the diagnosis. Inclusion bodies were found in only two.

In four cases immediate improvement occurred after local therapy, and in 14 to 21 days the follicles had disappeared and the pannus was less vascular. In the main, however, the long-standing pannus did not appear greatly altered, though all ulceration became inactive. Discharge and lacrimation ceased and the comfort of the patients has been greatly increased.

Two cases were slow in response and required systemic administration. After this, one improved considerably but the other showed little change. This last

was an unusual case in that, although the appearance was typical trachoma, the condition was unilateral and the patient had no symptoms except those from a slight ptosis. Now, 6 months after treatment, the follicles are less in number, but still present, and the pannus is unchanged. The patient remains symptom-free.

The above cases were not ideal material for clinical research, but there is no doubt that the improvement was very marked and immense relief was afforded to the patients.

Superficial Punctate Keratitis.—Eight cases of this condition were treated by local administration. In all except one there was subjective improvement during treatment, but in none was a cure effected.

Dendritic Ulcer.—Eleven cases were treated without result.

Keratitis with Lid Ulcer.—*This case does not fit into any of the above categories* but the results were so striking that it deserves mention:

> Ten days after vaccination (which resulted in a normal "take") acute conjunctivitis developed. When the patient attended hospital a corneal ulcer about 3 mm. diameter was found and an ulcer of about the same size on the lower lid. There was hyperaemia around this ulcer but the edges were not raised. A culture showed *Strep. viridans, Staph. albus,* and *B. xerosis.* Treatment with penicillin and atropine was given but after a week there was no improvement but rather deterioration. A second culture gave no growth. The patient was admitted to the ward and intensive local aureomycin given for 2 hours, after which the drug was applied hourly. After 36 hours the site of the lid ulcer was only marked by an area of hyperaemia and the cornea showed a minute stain. Aureomycin drops were continued hourly, and after a total of three days' treatment the condition was quiescent.

Whether or not this was a vaccinal kerato-conjunctivitis is difficult to say, but there is no doubt that aureomycin rapidly proved effective in curing a dangerous ulcer in which penicillin had failed to effect an improvement.

Disciform Keratitis.—Five cases of this condition were treated. Three cases treated by topical application only showed no improvement. Two treated by sub-conjunctival administration both improved: in one, this change for the better was only slight, but the condition is still gradually settling; in the other the state of the cornea improved rapidly and at the end of a fortnight appeared quiet. The last patient has now been observed for 10 weeks since treatment ceased and there has been no sign of further activity. The nebula is gradually clearing, the vision having improved from 6/36 to 6/18.

Discussion

The cases in this series were selected rather for their difficulty than for their simplicity. Only cases unresponsive to other drugs were treated.

The excellent results in certain cases of conjunctivitis and blepharitis are due to the wide field of action of aureomycin. Many bacilli and cocci insensitive to penicillin are sensitive to this abiotic, and in addition aureomycin is effective against certain viruses. With regard to conjunctivitis, it seems that aureomycin is particularly effective in those cases in which, although infection is obviously present, careful cultures reveal no organism. It may well be that such cases are due to virus infection. The cases of follicular conjunctivitis may also have a virus aetiology, as may the case recorded as "keratitis with lid ulcer". Trachoma, almost certainly a virus disease, also responded well.

Several reports of the effectivity of aureomycin in virus diseases

of the eye have appeared in the literature. Boase (1950) reports success in trachoma. Bellows (1950) and Bellows and others (1950) report successes in epidemic kerato-conjunctivitis. Sheehan (1950) mentions a cure in a case of presumed Newcastle (Philippine Fowl) disease causing conjunctivitis in a chicken farmer, though Gettes (1950) treated a proved case of Newcastle's conjunctivitis without success.

The previous report from this clinic described nine cases of dendritic ulcer in none of which local aureomycin produced a cure. Since this report only two further cases have been treated and they were also unsuccessful. These findings are in sharp contrast to those of Thygeson and Hogan (1950), who gave a 60 per cent. cure rate in from 4 to 7 days, and Zeller and O'Conner (1950) whose seven cases all healed.

The toxic effects of the drug when given orally are found to be more unpleasant than serious, and local application rarely causes any ill effects. In this series only one case of severe allergic reaction was encountered and this was with ointment. There was no case of allergy to the drops. It is to be noted, however, that Burstein (1950) reported an allergic response to guttae aureomycin 0·5 per cent. in a case with rosacea.

Summary

(1) Eight cases of resistant conjunctivitis were treated with aureomycin, six successfully.

(2) Thirteen cases of follicular conjunctivitis, four with corneal vascularization and ulceration, were treated; ten recovered.

(3) Ten of the fourteen cases of long-standing blepharitis treated were clinically cured. Eight of the successes were achieved by local administration only.

(4) Six cases of active trachoma received aureomycin; five showed great improvement.

(5) Superficial punctate keratitis did not respond to treatment given locally.

(6) A case of corneal ulceration and lid ulceration occurring 10 days after vaccination responded dramatically.

(7) Local administration of drops produced no benefit in three cases of disciform keratitis. Two cases received subconjunctival injection and one improved rapidly. Sufficient cases have not been so treated to give any conclusive results.

(8) Treatment of dendritic ulcers has not been successful.

(9) The value of aureomycin in external ophthalmological infections is considerable, particularly in conditions caused by

organisms resistant to the older antibiotics and in several types of infection caused, or presumably caused, by viruses. From the general point of view its therapeutic effect in trachoma is probably its most important application; long-term observations with pathological controls will be necessary before its true value in this disease can be properly assessed, but the preliminary observations are encouraging.

I wish to express my gratitude to Dr. Norman Ashton, without whose co-operation and assistance this work would have been impossible, and to thank members of his staff in the Pathology Department who have examined so many cultures and performed so many sensitivity tests. I should also like to acknowledge the help given by the pharmacist at Moorfields in preparing the ointments.

My thanks are due to the surgeons of Moorfields, Westminster and Central Eye Hospital for their kindness in referring cases for treatment.

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STREPTOMYCIN IN THE TREATMENT OF TUBERCULOUS ULCERS OF THE CONJUNCTIVA

A Further Communication*

BY

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IN a previous communication, Das Gupta and Usman (1949) described a case of bilateral symmetrical tuberculous ulcers of the bulbar conjunctivae, which responded very well to local parenteral streptomycin therapy. In that case no other tubercular focus could be detected. This article describes a case of tuberculous ulcers of the palpebral conjunctiva of one eye. The patient had other tubercular lesions elsewhere, which also responded well to streptomycin therapy.

Case Report

N. H., a male aged 19, Mohammedan student, resident of Ekbalpore (Bengal), was admitted to the Eye Infirmary, Medical College Hospital, Calcutta, on August 24, 1949, with ulcers in the upper and lower lids of the right eye.

History of Present Illness.—About two years ago the right eye showed an inflammation, more marked on the temporal than on the nasal side. After some days there was discharge from the right eye, and a few days later small ulcers were noticed on both lids, and these became gradually bigger. The left eye never gave any trouble.

History of Past Illness. About three years before his voice became hoarse. He attended the village dispensary and was given treatment but to no effect, and has now completely lost his voice. His appetite is poor and he has lost much weight.

Family History.—His parents are alive and quite healthy. He has five brothers and one sister, all healthy. He is unmarried and there is no history of contact with any tuberculous individual.

Diet.—He lives on an average Bengali diet of rice, wheat, vegetables, lentils, fish, meat, and milk.

Examination on Admission.—The patient was slightly built (weight 6¼ st.).

Right eye, lids swollen, with ulcers in both extending from the inter-marginal strip to the palpebral conjunctiva. In the upper lid the size of the ulcer was 13 × 5 mm., and in the lower 11 × 4 mm. The margins of the ulcers were clear cut, and there was a scanty whitish discharge over the surface. Cornea clear. No keratic precipitates. Pupil active to light. Tension normal. Vision 6/6. Fundus healthy.

Left eye, no abnormality detected. Vision 6/6. Fundus healthy.

The right pre-auricular and submental glands were enlarged. The temperature rose regularly towards evening, the maximum ranging from 100·6° to 101°F. Morning temperature was normal.

Investigations.—A scraping was taken from the floor of the ulcer on August 26,

* Received for publication June 21, 1950.

1949, and acid-fast bacilli were found. Discharge from the ulcer was sent for culture and was found to be sterile. Sputum was examined for acid-fast bacilli, with negative results. Sedimentation rate was estimated at 40 mm. per hour (Westergren). The blood was examined for total and differential count and the aldehyde and Chopra tests for kala-azar.

Blood Picture.—Total W.B.C.		9600 per c.mm.
Polymorphs		70 per cent.
Lymphocytes		26 per cent.
Large monocytes		2 per cent.
Eosinophils		2 per cent.
Malaria parasites		nil
Aldehyde and Chopra tests		negative

On September 7, 1949, the patient was sent to the Chest Department for a Mantoux test and skiagram of the chest. The latter showed nodular infiltration involving left apical and subapical regions. The Mantoux test was as follows:

(1) 0·1 ml. 1/1,000,000 dilution (O.T.); induration 8 × 8 mm.; reaction doubtful.

(2) 0·1 ml. 1/100,000 dilution (O.T.); induration 14 × 17 mm.; reaction + +.

On September 15, 1949, the patient was sent to the Ear, Nose and Throat Department, and extensive ulcerated areas involving pharynx, epiglottis, soft palate and base of tongue were reported.

On September 25, 1949, a section from the edge of the ulcer revealed tubercular granulation tissue, consisting of masses of epithelioid cells with areas of degeneration, lymphocytic and fibroblastic reaction.

FIG. 6.—Photomicrograph of section taken from edge of conjunctival ulcer (low magnification).

FIG. 7.—Photomicrograph of section taken from edge of conjunctival ulcer (high magnification) showing tubercular granulation tissue, consisting of masses of epithelioid cells with areas of degeneration, lymphocytic and fibroblastic reaction.

Treatment.—From September 2, streptomycin was given both parenterally and locally. 0·5 g. was injected intramuscularly twice daily. For local use 1 g. streptomycin was dissolved in 2 ml. distilled water and the drops given hourly from 8 a.m. to 8 p.m. After five days, the temperature came down and remained at normal. Altogether 40 g. streptomycin were given parenterally and 10 g. were used as drops.

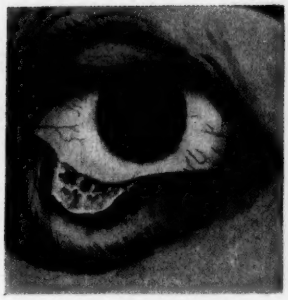

FIG. 1.—Before treatment, August 26, 1949.

FIG. 2.—After treatment, September 12, 1949.

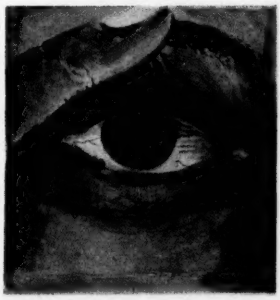

FIG. 3.—September 21, 1949.

FIG. 4.—October 18, 1949.

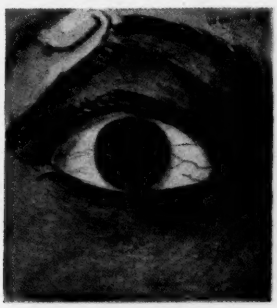

FIG. 5.—November 1, 1949.

Between September 9 and November 30, the weight rose from 6½ to nearly 7¼ stone. Between August 26 and October 24, the sedimentation rate fell from 40 to 6 mm. per hour. The vocal hoarseness almost disappeared and the general health improved greatly. On September 3 a scraping for acid-fast bacilli was taken again, with negative results. Figs 1-5 show how the ulcers improved during the course of treatment. Microphotographs of the section taken from the edge of the ulcer appear in Figs 6 and 7.

Summary

(1) A case of tuberculous conjunctival ulcer with other tubercular lesions elsewhere is described.

(2) This case responded very well to streptomycin therapy, given both parenterally and locally.

(3) Temperature came down to normal level within five days of beginning streptomycin treatment.

(4) Sedimentation rate dropped from 40 to 6 mm. per hour.

(5) The vocal hoarseness almost completely disappeared.

(6) The patient gained almost 1 stone in weight.

(7) No untoward symptom was observed during the whole course of treatment.

(8) For reasons beyond the author's control, culture for tubercle bacilli or guinea-pig inoculation could not be done.

I am very grateful to the Superintendent, Medical College Hospital, Calcutta, for allowing me to publish this case, to Dr. P. K. Sarkar, Pathologist, Eye Infirmary, Medical College Hospital, Calcutta, who did the microscopic section and all other laboratory investigations, to Dr. P. K. Sen, Physician-in-Charge, Chest Department, Medical College Hospital, Calcutta, for his valuable suggestions, and to Sri A. Das Gupta, who drew and painted the illustrations.

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USE OF TANTALUM DRAINS IN GLAUCOMA*

BY

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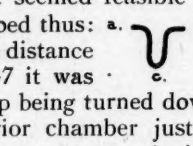
FOR as long as operative interference is necessary in glaucoma, so I suppose will ophthalmic surgeons try to devise new ways of reducing intra-ocular tension by drainage.

Recently the reading of an article (Bick, 1949) on the use of tantalum metal in drainage of the eye, has tempted me to submit this brief account of some efforts on my own part over the last few years to achieve successful intra-ocular drainage by the use of metal drains. Bick gives a comprehensive account of the use of foreign material implants in the eye for the purpose of drainage, from the earliest attempts of Rollet and Moreau (1906), who used a horsehair seton, to his own experiments in the same direction using implants of the metal tantalum.

These tantalum implants were used chiefly to keep open a supra-choroidal channel following a cyclodialysis, and he gives an account of four cases in which this procedure was carried out on human eyes. In three of these cases the implant had to be removed owing to a subsequent rise in tension. He concludes his article by affirming that the use of a tantalum drain is justifiable in desperate cases of glaucoma.

Accounts of tantalum—its inertness and its ready acceptance by human tissue without reaction—made me think that it might be used to keep open a small filtering scar in cases of high intra-ocular tension. I conceived it as more or less taking the place that the portion of iris in the wound does in the operation of iridencleisis.

The first idea that seemed feasible was to have a small piece of tantalum wire shaped thus: 

the distance from *a* to *b* being 4 mm., and the distance from the line *ab* to *c* being 3 mm. Early in 1947 it was tried out as follows: a small conjunctival flap being turned down, a keratome incision was made into the anterior chamber just behind the corneo-scleral junction and the loop *c* was gently inserted into it and pushed down into the anterior chamber until the whole little metal contrivance was supported by the arms *ab* projecting slightly on either side of the keratome incision. The flap was replaced with a suture.

* Received for publication July 10, 1950.

In the first few cases it worked well for some weeks, and then the tension began to rise again. There was no reaction to the metal at all—the iris was clean and quiet, and nothing abnormal could be detected by the slit lamp, except the bright glittering little loop lying quietly in the anterior chamber. Six cases were treated in this way, but after varying periods all six stopped draining. A trephine had to be done later, and in four the drain was removed. All one could find when removing the drain was that there appeared to be much scar tissue round the " arms " of the drain, which seemed to be the cause of the " sealing up " of the drainage wound. Two were left in, although trephined, and they are still there with no reaction whatsoever after two and a half years.

FIG. 1.—Tantalum drain.

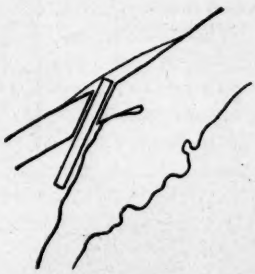


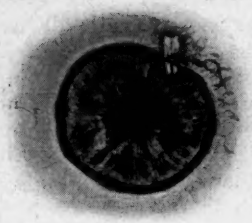
FIG. 2.—Sectional diagram, showing straight drain in position.

As the wire drain attained no permanence so far as drainage was concerned, and was yet so well tolerated by the eye, there seemed to be some prospect of gaining permanent drainage if one could design a better drain. Accordingly a drain was devised, which it was thought might give more permanent results by leading the aqueous further back into the tissues. This drain was in the form of a flattened tube—open down the back and tapering from back to front (see Fig. 1).*

It was hoped that this triangular form would fit into the triangular opening of a keratome incision.

The technique of inserting the drain was the same simple one : dissection of the conjunctival flap up to the corneal margin, small, very oblique keratome incision, insertion of drain, and reposition of flap. The position of the drain is shown in Fig. 2.

* These drains were beautifully made for me by Messrs. G. Nissel and Co., Ltd., Siddons Lane, Baker Street, London, N.W.1, meticulously polished and finished.



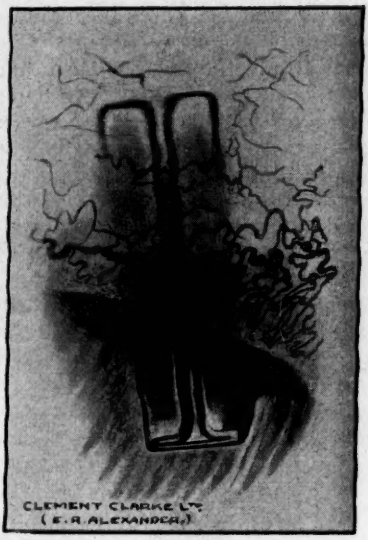
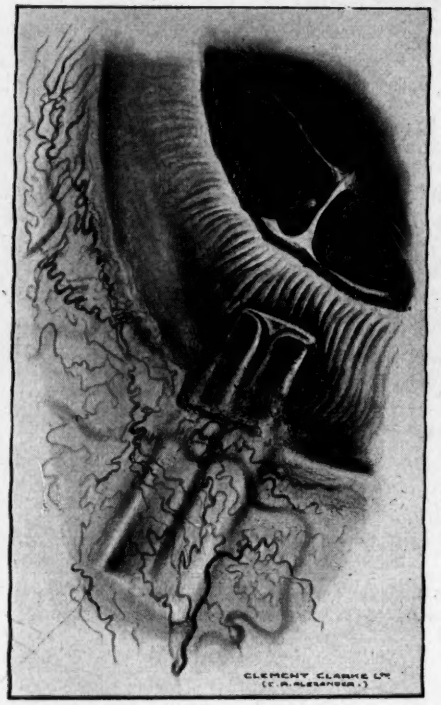


FIG. 3.—Drain in position, high and low magnifications.



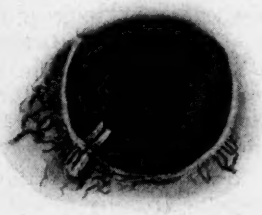


FIG. 4.—Drain in position, high and low magnifications.

In all, 25 of these drains have been used since 1948. No significant reaction has been found to any of them, though only two have kept the tension down for more than three to four months. Their use has, however, allowed cases of secondary and very advanced glaucoma, to be dealt with in the least traumatic manner possible.

Figs 3 and 4 show the drains in position in a case of old bilateral iridocyclitis with secondary glaucoma. These drains were inserted in June, 1949, and the tension in both eyes still remains low.

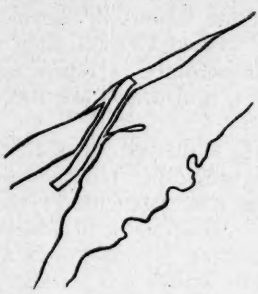


FIG. 5.—Sectional diagram, showing newer type of slightly curved tantalum drain in position.

I found with some of the original type of straight drain that the narrow end tended to dig into the iris, and I have latterly had some made by Messrs. G. Nissel with a double curve (like a very shallow S). These are much easier to insert and they accommodate themselves better to the curve of the sclera and to the incision, while they do not tend to dig so much into the iris (see Fig. 5).

In spite of the fact that the majority of cases tend to close up eventually so that the tension rises again, I have found these drains of much value:

(1) in acute glaucoma;

(2) in cases of high tension associated with iritis or iridocyclitis;

(3) in those cases of very advanced glaucoma with little visual field left, where one fears that the shock of a more drastic operation associated with sudden drop in tension may lead to final obscuration of vision. In these cases the trauma inflicted on the eye is the minimum possible, and when the tension has been lowered for some weeks and the eye is what might be termed "stabilized", a more permanent form of operation can be proceeded with in greater safety.

These few notes are proffered in the hope that others with greater facilities than are possessed here may be tempted to further and more successful experiments.

I am indebted to Sister G. Hughes of the Eye Department of the Caernarvonshire and Anglesey General Hospital, Bangor, for her help and suggestions.

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A CASE OF ONCHOCERCIASIS IN LONDON AND ITS TREATMENT WITH HETRAZAN*

BY

HAROLD RIDLEY and JOHN ANDERSON

London

ONCHOCERCIASIS is a disease frequently overlooked in endemic areas and this case is a reminder that the diagnosis should be considered even in England when ophthalmic lesions of obscure aetiology are found in patients who have visited Central Africa or Central America. It also shows the importance of repeating laboratory investigations in suspected cases, and draws attention to recent advances in chemotherapy.

It will be recalled that onchocerciasis is a disease caused by infection with the microfilariae of a threadworm, *Onchocerca volvulus*. These enter most parts of the eye, particularly the cornea, the uveal tract, and the optic nerve, leading to blindness from corneal opacities, complicated cataract, choroido-retinal degeneration, and optic atrophy. The adult worms are generally found in subcutaneous nodules. Infection is carried by a fly, *Simulium*, which breeds in running water.

A medical colleague told us that his brother, aged 35, a District Officer home on regular leave from Northern Nigeria, had for two months complained of a pricking sensation in the eyes, and of photophobia, and had been found to have a number of punctate opacities in both cornea, the cause of which was obscure. There was also a history of transient attacks of irritable oedema in the limbs. The possibility of onchocerciasis was considered and the patient was brought to St. Thomas' Hospital.

He was found to have slight conjunctival injection without discharge, and photophobia severe enough to make slit-lamp examination difficult. Though the visual acuity of each eye was 6/5, both cornea contained about 20 nummular opacities, 0·5 to 1 mm. in diameter, scattered diffusely in the superficial substantia propria. These plaques were not most numerous in the nasal interpalpebral area, as generally happens in onchocerciasis, and no dead microfilariae were seen within them. Nor on any occasion were living microfilariae seen in the anterior chambers. Thorough examination failed to reveal any onchocercal nodules.

A 4 per cent. cocaine drop instilled into the conjunctival sac appeared to cause undue irritation, and a fragment of bulbar conjunctiva about 3 mm. in diameter was excised from the left

* Received for publication June 8, 1950.

eye. This specimen was unfortunately not examined microscopically before fixation, so that the opportunity of finding living worms was missed. Numerous coiled bodies suggestive of dead worms were seen, but no one was convinced that these were indubitably microfilariae, especially when a similar conjunctival snip taken from the other eye proved negative. The next two snips from each eye were also free from microfilariae, as were several skin snips taken at random because no suggestive nodules were found. Centrifuged specimens of blood taken at midday and midnight contained no microfilariae, but an eosinophilia of 24 per cent. was present. The patient returned for further examination one week later, and two more conjunctival snips were taken immediately after the instillation of one drop of cocaine. It was thought that the excessive irritation caused by cocaine might be due to live microfilariae escaping from the drug, for it is known that the adult loa loa retreats into the orbit when the conjunctiva is anaesthetized. The specimens were placed in a drop of normal saline and examined immediately; one living microfilaria was seen which when stained proved to be *Microfilaria volvulus*, thereby establishing the diagnosis.

Until recently no treatment other than excision of nodules has had any real value in the eradication of adult worms and microfilariae. Animal experiments have shown that antimony preparations such as stibophen are filaricidal only in doses toxic to the host. Recently Hewitt and others (1947) have reported on the use of hetrazan in filarial infections. This drug, which appears to be of very low toxicity to man, is microfilaricidal, but has little effect on adult worms. It is especially active against *Mf. volvulus* and *bancrofti*. In an infected person, however, the first doses usually produce considerable reaction which is presumably due to sudden death of numerous microfilariae.

It was decided to try hetrazan hydrochloride in this case, but because many authors report brisk reactions with oedema and irritation of the skin, and stress the need for caution where the eyes are involved, it was decided to give an antihistamine drug before starting hetrazan, and to begin with small doses rapidly increasing to the maximum after observation of effects.

The treatment was given as follows:

25.4.50. 26.4.50.	50 mg. phenergan 4-hourly.
27.4.50.	phenergan as above + 12·5 mg. hetrazan hydrochloride.
28.4.50.	12·5 mg. phenergan + 25 mg. hetrazan hydrochloride.
29.4.50.	phenergan + 100 mg. hetrazan hydrochloride.
30.4.50.	phenergan + 50 mg. hetrazan hydrochloride.
1.5.50.	phenergan + 100 mg. hetrazan hydrochloride.
2.5.50.	150 mg. hetrazan hydrochloride three times. This dose was continued for a total period of ten weeks.

Increased oedema, a small papular urticarial eruption, oedema of the arms, legs, and face, and increased photophobia together with fever up to 100° F. were noted. No lung-field changes at the height of this reaction were found in the x rays, and the eosinophilia in the blood remained constant (3,360 per c. mm.—24 per cent. of 14,000 white blood corpuscles). This reaction subsided in 8 days. The results achieved appeared to be satisfactory one month from the start of therapy, and the patient thought himself normal. The eyes were no longer injected and irritable, but the corneal opacities were still present. It was thought desirable and safe to continue with hetrazan hydrochloride 150 mg. three times a day for a total period of 10 weeks.

Proof of cure could not be obtained in this case by skin snippings after treatment, because these were negative for microfilariae throughout. It is suggested that a trial course of hetrazan hydrochloride 3 months after the end of the present course may establish persistence of the disease or cure, by producing or failing to produce a similar reaction to that described here.

Our thanks are due to Dr. J. L. Pinniger for performing the pathological examinations.

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ALACRIMIA CONGENITA*

BY

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ALACRIMIA CONGENITA seems to be a very rare disease. We have succeeding in finding only nine cases in the literature. There is scant reference to the aetiology of the condition and the incidence of kerato-conjunctivitis sicca as a sequel is described only in single cases.

The first case of congenital absence of lacrimal secretion was described by Morton (1884):

> Bertie L., *aet.* 6, has been noticed by his parents never to shed tears from the right eye. On several occasions I have seen him crying, and though the tears flowed copiously from the left eye, they never came from the right. That they were not secreted was demonstrated by drawing away the lower lid from the globe, when there was no accumulation of tears in the cul-de-sac thus formed. In the left eye the vision is normal, but in the right, even with the necessary correction of + 0·5 D sph. + 2 D cyl., it was not more than 20/50. The pupils act well and equally, and there is no impairment of colour vision or of the senses of touch, taste or smell on the right side. The boy's face is somewhat flatter and the external orbital angle and malar bone less developed on the right side than on the left. The right eye also appears smaller than the other. The right ear is slightly "lopped", and the upper part of the cartilage is thinner than on the left side. The mother has "harelip" on the right side, but there is no other history of deformity, and there are two younger children quite healthy. The lacrimal gland cannot be felt on either side, but it seems a reasonable assumption that it is congenitally absent on the right side.

Heubner (1900) described a boy, aged 1½, with healthy parents, who suffered from double-sided paralysis of the abducent, facial, and hypoglossal nerve, the left side being more affected than the right, with a complete lack of tears. At the examination post-mortem Heubner found that the cause was a congenital aplasia of the brain where the nuclei of these nerves lie. Thus the left hypoglossus, left facialis, and both abducens nuclei were lacking, and in the right hypoglossus and facialis nuclei the cells were fewer than usual.

Sommer (1903) described a child aged 2½ who had never shed tears. He came from a healthy family, and was physically and psychically normal. On examination of the eyes the conjunctiva was found to be normal. Irritation of the conjunctiva, cornea, or the nasal mucous membrane produced no secretion of tears, and the eyes became only a little moistened. The function of the salivary glands was normal.

According to Sommer there is reason to suppose that the case

* Received for publication June 14, 1950.

represents an abnormally long persistence of a physiological condition found in new-born children during the first weeks.

Coppez (1920) described a 2-year-old child with epicanthus and double-sided ptosis who had never shed tears.

Kayser (1921) reported a case of congenital trigeminal paralysis with total lack of tears. The child belonged to a family in which there appeared a series of congenital dystrophies. In this patient the eye symptoms began nine days after birth with small, round defects in the cornea healing quickly and leaving small scars. The process lasted till death at the age of 3½ years. Conjunctiva and cornea were completely insensitive and the eyes dry. Tears had never been observed.

Ishikawa (1928) mentions a 4-year-old boy with no family history who lacked tears since birth. The conjunctiva was dry and slightly hyperaemic. The cornea was normal. Strong emotions and local irritation (*e.g.*, foreign bodies in the conjunctiva) failed to provoke tears. The case was explained as a congenital hypoplasia of the lacrimal gland.

Duke-Elder (1930) described a 5½-year-old child who had lacked tears since birth. During the first years there had been a viscous secretion from the eyes and photophobia. Both eyes seemed normal, apart from the cornea. In the deeper epithelial layers, and at some points penetrating into the superficial part of substantia propria, there were several small opacities, especially in the lower segments of the cornea. The corneal sensibility was normal. The lacrimal secretion, measured with Schirmer's test, gave sub-normal values. Stimulation by substances with strong odour also gave sub-normal values.

Bruce Hamilton (1940) described an 11-months-old child who completely lacked tears when crying. No moisture was present in the conjunctival sacs. The corneal sensitivity was poor and central keratitis was present in both eyes, with considerable areas of staining. The changes in the eyes quickly healed after obliteration of the lacrimal canaliculi.

Riddell (1940) described a 5-year-old girl who had never been able to cry, but here there were no other changes in the eyes.

Case Report

The present authors have recently examined a 5-year-old girl who had always lacked tears and showed symptoms of kerato-conjunctivitis sicca.

The patient's parents were healthy and not related. There were no known diseases in the family, particularly of the eyes, and the patient, an only child, born at term, had always been healthy. The mother told us that the girl had never produced tears on crying. The eyes became a little moistened, and the skin above them and on the forehead a little red. The child had never complained of eye symptoms and had no photophobia.

Ophthalmological Examination.—Fundi normal. Visual acuity 5/5. Corneal sensitivity normal. Corneae covered with a viscous secretion containing epithelial

cells. In the conjunctival sacs was found a scanty, tenacious secretion that could be drawn out in long threads. With rose bengal the conjunctiva and cornea became faintly but distinctly stained. Groups of epithelial cells with strongly coloured nuclei were also seen.

Schirmer's Test I: right, 1·5 mm.; left, 0·1 mm.

II: (NH_3) right, 3·0 mm.; left, 0 mm.

Tear-Gas Test: The test with tear-gas was made in a closed room, with four persons present besides the patient. All had an abundant flow of tears, but the patient's eyes remained dry in spite of psychical crying owing to pain in the eyes. The pain made it impossible to carry out Schirmer's test at this experiment.

The palpebral lacrimal gland was of normal size and appearance.

General and Neurological Examination

Blood: Hb. 80 per cent. R.B.C. 4·44, W.B.C. 4600. Blood picture normal. Erythrocyte sedimentation rate, 7 mm. per hour. Wassermann reaction negative. Glucose-tolerance test, water-balance test, and basal metabolism normal.

Test Meal: No free HCl; fraction test showed free HCl.

X-Ray Examination: Cranium normal.

Oto-rhino-laryngologic Examination: Nothing abnormal. Salivary secretion normal.

Discussion

Thus in a child healthy in all respects, we found an absence of lacrimal secretion, even after irritation with tear-gas. Clinically there was the picture of kerato-conjunctivitis sicca. Microscopic examination of a piece of the conjunctiva bulbi showed oedema with early hydropic degeneration of the epithelium (Figure).

Microscopic examination of a piece of the palpebral lacrimal gland showed a normal picture. After obliteration of the lacrimal puncta the clinical signs disappeared.

FIGURE.—Section of conjunctiva bulbi. Oedema with beginning of hydropic degeneration of the epithelium.

Of the ten cases reported above, four have shown changes of the kerato-conjunctivitis sicca type. However it should be observed that in the first six cases the description was incomplete and belongs to a time when this disease was unknown. In four cases information is lacking, and in two it is reported that the eyes were normal. Thus it may be said that the characteristic hydropic degeneration of the conjunctival epithelium may appear even among children where the lacrimal secretion is lacking from birth. However, we do not know how long it takes before kerato-conjunctivitis sicca develops.

With regard to the cause of the lack of tears there are different possibilities. Morton (1884), whose case was unilateral and showed a series of facial anomalies on the affected side, considers it probable that the lacrimal gland was missing on that side. Lutz (1931) pointed out that here the cause might be an aplasia of the petrosal bone with co-existing aplasia of the nervus petrosus superficialis major. Coppez (1920) and Ishikawa (1928) believed that the condition was due to a congenital hypoplasia of the lacrimal glands. However, it has not been possible to prove this. Kayser (1921) sees the cause in a congenital paralysis of trigeminus. Heubner (1900), whose case showed paralysis of several cranial nerves, proved microscopically an aplasia of the nervous nuclei.

In our case no nervous symptoms could be proved and the lacrimal gland was microscopically normal. It is difficult to decide the cause of the lack of lacrimal secretion in this case. Apart from the missing lacrimal secretion, no hypofunction of the secretory organs, and no other morbidity, was proved.

The newborn child does not secrete tears when crying, for the nervous paths connecting the psychical reaction with the lacrimal centre only develop after some weeks. As a rule, however, the reflex secretion of tears functions from birth. We find in a few older investigations (Kirschstein, 1894; Axenfeld, 1899) the information that, at least in certain cases, the reflex lacrimal secretion is lacking or is very little marked, just after birth. In this respect new researches seem to be necessary, but it does not seem quite absurd to agree with Sommer (1903) and to see the cause of at least some cases of congenital alacrimia in a failure to establish a connexion between the nervous pathways and the lacrimal centre, which produces an alacrimia congenita persistens. We may see an analogy between this and, for example, the congenital lack of fusion which in certain cases becomes permanent and is the cause of strabismus.

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SYMPATHETIC OPHTHALMITIS OF UNUSUAL ONSET

A Further Report*

BY

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IN 1948, we described a case under the above title. In December, 1945, the injured right eye developed an iridocyclitis of severe type and later had to be removed. In March, 1946, the left eye developed signs of papillitis and mild uveitis, mainly posterior, which after treatment resolved almost completely, and by June, 1946, vision was restored to 6/5. After three years we now have to report a disappointing sequel.

Case Report

The patient, a European farmer, aged 57 years, was re-admitted on January 27, 1949, to the Groote Schuur Hospital, Cape Town, with a red and painful left eye. On examination he was found to have an acute iridocyclitis, with a heavy exudate in the anterior chamber.

History.—Since his discharge in June, 1946, the patient had been free from trouble, except that on a few occasions there had been periods of blurred vision and watering of the eye without pain. It was difficult to establish definite evidence of these attacks because no doctor saw him until about one week before admission when the eye had become painful and the vision blurred.

Course and Treatment.—On admission, heroic treatment was instituted without delay. Intravenous calcium gluconate and N.A.B. were given, as well as 200,000 units of penicillin intramuscularly, followed by 100,000 units at 6-hourly intervals for five days. By mouth, sodium salicylate was exhibited. He received, in addition, the usual local applications, as well as sedatives.

At the same time a search was instituted for some hidden infective cause for this new attack. His jaws (edentulous), were *x*-rayed for root stumps, and tonsils, ears, and sinuses were investigated, with negative results. The honorary venereologist to the hospital reported that the left seminal vesicle was indurated and that the secretion obtained by massage showed numerous pus cells, and also expressed the view that "iridocyclitis was more often due to infection than to syphilis". (The Wassermann reaction was negative.) On his advice daily diathermy to the perineum and bi-weekly vesiculo-prostatic massage were instituted.

In the course of the next six weeks the patient received 12 million units of penicillin as well as 12 gm. of streptomycin, followed by 120 grains of salicylate daily for five days, and then 14 gm. of sulphatriad over 48 hours. Short intensive courses of salicylate were repeated at intervals. On May 27, it was decided to do a bilateral vasotomy with a view to establishing drainage in the vaso-urethral tracts. These were reported patent, but by June 8, the left seminal vesicle was still indurated, with a moderate number of pus cells in the secretion.

The intra-ocular inflammation, however, pursued a relentless course. In the early part of treatment there appeared to be some slight improvement, but at the

* Received for publication September 14, 1949.

end the cornea had cleared only a little, the iris was atrophied and the plug of exudate in the pupillary area had largely absorbed, leaving a densely cataractous, swollen lens projecting through a wide pupil. Pain and tension subsided to some extent. On June 26 the patient was sent home, certified blind.

Discussion

This case presents a problem in diagnosis. The course of uveitis was clinically indistinguishable from that usually known as sympathetic ophthalmia. In this respect its failure to respond to the formidable exhibition of all the antibiotic drugs at our disposal, as well as several well-tried non-specific adjuncts, was characteristic. In the early stages of this case in 1946 one was never in any doubt as to the diagnosis after the original inquiry. The fact that the sympathizing eye cleared eventually to a point where vision returned to normal and all evidence of active inflammation had subsided led one to believe that the condition had been controlled permanently.

The question that arose subsequently was whether the final destructive process was a relapse of the same condition, or whether it was due to some other, probably infective, cause acting on an eye already the subject of iridocyclitis. If the former, an interval of nearly three years between two distinct attacks must be extremely rare, if not unknown. The literature gives several instances of a protracted course with rather frequent relapses, sometimes over a period of years. Duke-Elder (1940) quotes a report by Verhoeff, whose case had eight relapses in 8 years. The usual tendency is for each successive attack to leave the eye a little more crippled. We have been unable to find a record of a similar case with a quiescent interval of anything approaching three years. It is possible, however, to regard the episodes of reduced vision and slight discomfort of which the patient complained as minor relapses within that time. These symptoms form the only link between the two main episodes and must be taken into account. On the other hand evidence is not wanting that unsuspected infection, especially in the lower genito-urinary tract, is a potent cause of chronic uveitis. Here there was evidence of such infection. It is more logical to postulate repeated attacks from such a focus of infection than to regard the case as a form of protracted sympathetic ophthalmia.

Finally, can one assume that the first attack was sympathetic and the last infective in nature? At the time of the first attack there was no doubt clinically as to the type of iridocyclitis present and no special search for focal infection was made; this was only done subsequently in view of the long interval between the main attacks.

Summary

(1) A case of unusual sympathetic ophthalmia in the sympathizing eye (the exciting eye having been removed), which resolved to a completely quiescent state, but succumbed subsequently to a severe progressive uveitis indistinguishable from typical sympathetic inflammation.

(2) There was an interval of nearly three years between these two attacks.

(3) Chronic latent infection in the prostate and vesicles was demonstrated.

(4) The treatment included astronomical doses of penicillin, streptomycin, sulpha-drugs, and salicylates without any appreciable effect. Treatment on similar lines was thought at first to have controlled the original attack.

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APPLIANCE

STERILE ANTERIOR-CHAMBER IRRIGATION*

BY

L. G. SCOULAR

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NO matter what type of operation is employed when extracting a cataract, it is often necessary to wash out the anterior chamber. In doing this it is obviously important that the solution used should be sterile.

As a general rule normal saline is employed which has been made up by the hospital dispenser and stored in glass-stoppered bottles. As these are not sterile on the outside, the usual procedure is for a nurse who has not scrubbed up, to pour the saline into a sterilized undine or container. In doing this there is a very good chance that she will contaminate the neck of the bottle with her fingers and so infect the solution. If it is not infected in this way there is every possibility that it will become so through exposure to the air.

The following is a simple method which is practically foolproof. The illustration shows a 4-oz. "American round" bottle with a metal screw cap. In the top of the cap there is a hole 9 mm. in diameter which is covered by a rubber disk. This bottle is two-thirds filled with normal saline and can be sterilized in an autoclave or placed in a sterilizer along with the instruments before the operation. When the surgeon is ready to irrigate the anterior chamber two sterile needles are passed through the rubber disk. One of these is a long fine needle which should be more than half the length of the container. The second is a short wide-bored needle connected to a length of rubber tubing on the other end of which is the anterior-chamber irrigation nozzle. When the bottle is inverted, air passes in through the long needle and the saline runs out through the short needle and along the tube. It is necessary to make sure that the short needle has a sufficiently wide bore. If it is too narrow the flow is not adequate.

Another advantage of this method is that, if it is necessary to irrigate a second time, the saline starts to run immediately without being preceded by numerous air bubbles as invariably happens when using an undine.

* Received for publication July 14, 1950.

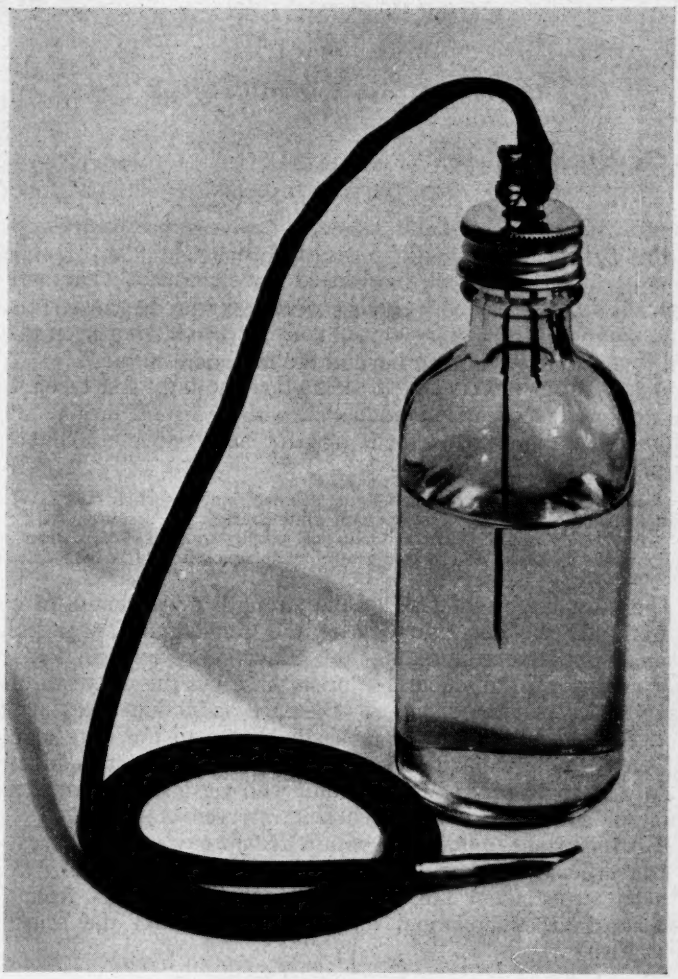

FIGURE.—Sterilized normal saline container with needles in position.

CORRESPONDENCE

CONVERGENCE DEFICIENCY

To the Editorial Committee of

THE BRITISH JOURNAL OF OPHTHALMOLOGY

DEAR SIRS—Dr. Mellick's article, " Convergence Deficiency ", in the *British Journal of Ophthalmology* (1950), **34**, 41, raises some questions which may well need to be clarified. The author does not say how the convergence weakness was diagnosed; there is no mention of the near-point of convergence having been taken and found to have receded beyond the minimum normal.

In fact, from the context it seems that the only test taken was the prism convergence or adduction with a *distant* target. One infers this from the statement that for near one must converge 21 prism diopters.

> " Individuals who are capable only of this degree of adduction [*i.e.*, 21△] are employing their maximum convergence continuously . . . at near ".
>
> " Apparently there exists a group of people with even less than this minimum (21△) who do not complain of symptoms referable to their defective convergence ".

The most important test for the strength or weakness of convergence is the determination of the convergence near point. Next in importance is finding the convergence reserve, *i.e.*, the *near* adduction, the amount of prism base out the eyes can overcome at the reading distance. Distance adduction gives at best a very indirect and often a misleading clue to the state of convergence. One will often see patients whose distance adduction is only 10 to 15 prism diopters, and who yet have a normal near point of convergence and sufficient reserves at near.

It is important to note that with a *distant* target the innervation to converge, to overcome prism base out, is only fusional. With a *near* target there are the additional innervations from the associated accommodation, and, above all, from the sense of nearness.

Yours faithfully,

JOSEPH I. PASCAL, M.D.

37 WEST 97TH STREET,
NEW YORK 25, N.Y., U.S.A.

May 22, 1950.

THE following notes have been received from the contributor:

To the Editorial Committee of
THE BRITISH JOURNAL OF OPHTHALMOLOGY

DEAR SIRS—The diagnosis of convergence deficiency was made by determining:

(1) The near point by means of the Livingston binocular gauge.
(2) The convergence at the reading distance on the synoptophore, adding base out prism to the blur point and then to diplopia. Recovery point was also noted.

Although the near point of convergence should be measured in every case, from the point of view of causation of symptoms more reliance should be placed on the findings at the reading distance. The existence of a group of asymptomatic convergence deficients has been noted before.

A. MELLICK, M.D.

26 SANDYFORD PLACE,
GLASGOW, C.3, SCOTLAND.
June 19, 1950.

TRIAL LENSES

To the Editorial Committee of
THE BRITISH JOURNAL OF OPHTHALMOLOGY

DEAR SIRS—The present commercially available types of trial lenses are, in my opinion, undesirable in one respect. The opaque rim of the small-aperture lens precludes observation of the patient's eye during refraction; in particular it prevents the surgeon from seeing whether the patient is "screwing the eye up".

Before the war one firm made large-aperture lenses with plastic rims, and these were, in my opinion, very satisfactory. It is no longer possible to obtain these, and manufacturers whom I have approached say that they will not be made again unless there is a sufficient demand by ophthalmologists. Either a large-aperture lens in any rim, or a small-aperture lens in a transparent rim, would meet the need; for other reasons the latter type is the the better. It is possible to have a special set made, at a price, but quantity production is needed, and this can only be obtained if support is forthcoming.

I note also that in new trial cases the lens-racks carry the lenses so close together that their removal is difficult for the average finger and thumb. This is an unnecessary obstacle.

I have brought this to your notice in the hope of support from other ophthalmologists, and I shall be glad to hear from any who are interested.

Yours faithfully,

NIGEL CRIDLAND.

25 CRANESWATER PARK,
SOUTHSEA, HANTS.
November 7, 1950.

To the Editorial Committee of
THE BRITISH JOURNAL OF OPHTHALMOLOGY

DEAR SIRS—I read Mr. Cridland's letter with interest and would add one advantage of the large-aperture lenses, which is that with them one can test children on the amblyoscope, whereas with the small-aperture lenses and a squint of more than a few degrees, the squinting eye is apt to be obscured by the rim.

On the other hand, there is no doubt that for handling and general convenience the small-aperture lens with the wide rim is better, and speaking personally, I would prefer it to the large one for these reasons.

When I first obtained a set of small-aperture lenses I too found that the lenses seemed to be too close together. I am never conscious of this now, and assume that it is just a matter of practice to accustom oneself to picking them out.

Yours faithfully,

F. A. WILLIAMSON-NOBLE.

27 HARLEY STREET,
LONDON, W.1.
November 15, 1950.

BOOK NOTICES

Essentials of Ophthalmology. By RONALD J. PRITIKIN. Pp. 651, + xi, 215 illustrations, including 18 in colour. J. B. Lippincott Co., Philadelphia and London. 60*s*.

Authors who include anatomical descriptions within the covers of a text-book mainly dealing with clinical matters have often been criticized on the ground that readers seeking such information will consult separate works on anatomy. But will they? Perhaps no library is available at the crucial moment, and so the reader plunges deeper into misconception, for lack of access to anatomical pictures whereby the account of a disease might be clarified. Many a student will bless Dr. Pritikin for setting out at the beginning of his book not only the essentials of the anatomy of the visual apparatus, but also a résumé of development and physiology in relation to these organs. Objective and subjective methods are carefully described with the aid of numerous helpful diagrams and photographs, and the author then proceeds to pack a mass of helpful information about orthoptic principles and deranged function of the extra-ocular muscles into a single chapter. Then he deals lucidly with optics, industrial ophthalmology and elementary medical jurisprudence before going on to diseases of the eyelids, lacrimal apparatus, eyeball, and orbit. Only a few pages remain for the ocular manifestations of general disease, but here again Dr. Pritikin contrives to supply a host of important facts within a small space.

A few minor alterations should be made in subsequent editions. Thus on pp. 31-2 we read: " In the macula only modified cones are present in the rod and cone layer ". That statement correctly applies to the juxta-foveal region, but not to the whole macula. It is unnecessary to use a toothpick or match, as recommended on p. 276, in order to evert the upper lid. Perhaps swimming-pool conjunctivitis can be caused, as the author states on p. 230, by staphylococci or Gram-positive bacilli, but authorities on each side of the Atlantic are nowadays more inclined to blame a virus issuing from female genitals. On p. 380 we read of " a brilliant multicolored ring " of corneal pigment in hepato-lenticular degeneration. The typical ring at the periphery of Descemet's membrane in these cases is golden-brown, not variegated. A chart on p. 174 correctly indicates the action of the extra-ocular muscles, but Table I on p. 15 might easily give rise to misunderstanding, because here the main action of the superior rectus

is described as " up; up and out ", that of the inferior oblique as " up and in ", and so on with the other vertically-acting muscles. No doubt Dr. Pritikin is here pre-occupied with the fact that the superior rectus elevates most effectively when the eye is abducted, and *mutatis mutandis* the same can be said of the other three muscles concerned. Nevertheless it is misleading to say, *e.g.*, that the superior oblique's main action is to move the eye " down and in ". The superior oblique is an abductor, as is made clear on p. 174.

These minor faults are here mentioned with constructive intent, because Dr. Pritikin deserves warm congratulations upon this well-planned introduction to ophthalmology, clearly printed upon good paper, and adorned with excellent illustrations. One particularly delightful item in the histological exhibition at the International Congress this year was a display of work done by the author and his colleagues upon the bacteriology of ocular infections in Mid-west, U.S.A. His exposition of the specimens showed him to be an acute and enthusiastic observer, and that same quality emerges as a notable feature of the disease-descriptions in this book, which may confidently be recommended as a broad introduction to the study of the eye in health and disease.

Surgery of Cataract. By DANIEL B. KIRBY. Pp. 695, 339 illustrations, including 21 coloured plates. J. B. Lippincott Co., Philadelphia and London. 1950. £12 ($30).

Daniel Kirby, by reason of his writings, his lectures abroad, and his professional hospitality in New York, is now generally recognized as one of the foremost technical exponents of the surgery of cataract. It is good that he has had the time and energy to put on paper the results of his experience, and the result is an interesting and refreshing book. It is unusual in many ways, not the least being the stress given to the historical development of the subject from its earliest beginnings some 3,000 years ago to its highest technical culmination to-day. The whole is lavishly illustrated and a gallery of pictures shows us the likenesses of the great figures who have moulded thought on this subject, from Susruta, father of Hindu surgery and Hippocrates, Celsus, and Galen, to the most notable modern exponents of cataract surgery.

The substance of the book is divided into five parts: the development of cataract surgery, the preparation of the patient, the techniques of the various operative methods, and two comparatively small sections discussing respectively the correction of

aphakia and the visual results obtained after removal of the lens. The book is not a one-sided exposition of the author's views, for others are abundantly quoted, but its greatest value lies in the author's appreciation of the drama of this branch of surgery, his realization of the importance of the minutiae of technique, his ingenuity in obviating and surmounting difficulties and complications, and not least, in his own original contributions to the subject.

The book is the result of immense experience, profound thought, and an unusual technical originality. It will repay reading, not only for the wealth of sound advice which it contains, but also as a demonstration that a book on surgery can be as interesting and as exciting as a detective novel.

Ophthalmic Operations. By SEYMOUR PHILPS. Pp. 390, + viii, 510 figures. Baillière, Tindall, and Cox, London. 1950. 50*s*.

This excellent book is so well written and illustrated that it is bound to go through several editions. The statement that conjunctival cultures may be dispensed with in all but cataract operations will come as a shock to some, but for very many years at one London Ophthalmic Hospital no culture was ever done even for a cataract. The eye was padded for 24 hours and the condition of the conjunctiva a short time before operation decided whether it should be performed. The careful detail put into the description of the pre-operative preparation of the skin, the application of towels and masks, and the lay-out of the instrument trolley, together with numerous helpful photographs, make this section of very great value. No truer word has been written than

"A good nurse . . . cannot be good at her job unless she is interested in it, and she cannot be interested unless someone has taken the trouble to tell her what is the problem in that particular patient, what is hoped for, and what complications may arise. This is a very different thing from attending a series of set and impersonal lectures. . . ."

It will be a good thing for ophthalmology when this attitude is more generally adopted.

One always looks in vain for some estimation for the guidance of house-surgeons regarding the length of time the patient should be in bed and in hospital for each particular operation. These periods would vary with different surgeons but it would be useful to know the ideas of the author on this subject. He has given such advice in the case of a few operations but not frequently enough. Another helpful thing would be a statement as to which operations, as, for *e.g.*, a needling of after-cataract, may be done without admitting the patient.

There are signs of hurried proof-reading in the captions of the

illustrations. In giving the complications after cataract extraction, the author has omitted to mention expulsive haemorrhage. The role of arteriosclerosis in the production of a vitreous haemorrhage after diathermy for detachment has not been evaluated. In operating for detachment, he says, " diathermy too near the ciliary body will cause an inflammatory reaction in the tissues, and unless the pupil is kept widely dilated, posterior synechiae will result ", but in describing cyclodiathermy this point is not mentioned. Perforating cyclodiathermy should have been noticed even if only to condemn it. These small criticisms have, however, but a minor importance, and in no way detract from a really valuable contribution to operative literature.

Vision: Its Development in Infant and Child. By A. GESELL. Pp. 329 + vii, 72 figures. Hamish Hamilton, London. 1950. 42*s*.

As Director of the famous Clinic of Child Development at Yale University, Dr. Arnold Gesell has what are perhaps unique facilities for the study of infant and child behaviour. He has written several books surveying behaviour from the 28th week of intra-uterine life through infancy and childhood until the age of 10 years. He has made use of the facilities of his clinic to study behaviour patterns, tests of visual skills, and the growth of visual functions and their relation to the total make-up and behaviour pattern of infant and child. His present book has been produced with the collaboration of his ophthalmic associates and describes observations on visual function for the first 10 years of life.

In the introductory chapters the authors emphasize the intimate interfusion of the visual and action systems of the body, and describe briefly their earlier observations on child progress. The original study of child behaviour took into account the four major fields: (1) motor behaviour, (2) adaptive behaviour, (3) language behaviour, and (4) personal-social behaviour. The methods by which the data were accumulated are briefly described, but the reader is referred to earlier works for more detailed information. In a short historical survey of the evolution of the human action system, the development of visual function and the optic apparatus from the lower chordates up to man are briefly sketched. In the concluding chapter of the introduction the reader is reminded of the essential physiological features of the motor basis of vision.

The main section of the book is divided into three parts: (1) the growing action system, (2) developmental optics, and (3)

developmental appraisal. These aspects of visual behaviour are approached in an entirely original manner, and the views of the author and his associates are supported by a wealth of clinical observation and the results of patient research. It is fascinating to follow with the writer the course of visual development, stage by stage, each chapter adding new associations between visual function and behaviour patterns, as the reader is taken through the years of infancy and childhood. Cognisant of the interest engendered by the visual stimulus, the author has taken full advantage of the medium of photographic illustration to make clear by pictures what it is often difficult adequately to express in words.

Whether the book justifies the mass of painstaking work and patient investigation which its author and his associates must have undertaken is for the individual reader to decide, but whatever opinion he may form, he will have enjoyed his perusal of this original and attractive volume.

Reviewed in *Ophthalmic Literature*.

Blindness. Multiple authorship, edited by P. A. ZAHL. Pp. 576 + xvi, 21 plates, bibliographies. Princeton University Press, U.S.A. Geoffrey Cumberlege, London. 1950. 40s. ($7.50).

A comprehensive volume dealing with the history of blind welfare, the education and psychology of the blind, their vocational rehabilitation, particularly as applied to the military blinded, and the devices, past and modern, to aid their rehabilitation.

NOTES

MEETINGS

THE Annual Meeting of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Gizeh, Egypt, on March 15 and 16, 1951. Medical practitioners, both ophthalmologists and others, are cordially invited. Further information may be had from the Honorary Secretary, Dar El Hekmah, 42, Kasr El Ainy Street, Cairo, Egypt.

The Eleventh International Dental Conference will be held in London from July 19 to 26, 1952. Further details may be had on application to the Honorary Secretary, 13, Hill Street, London, W.1, England.

HONOURS

H.M. THE KING OF EGYPT has conferred the title of Bey upon Dr. Mohamed Khalil.